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**Lower Section Room, Municipal Auditorium, Springfield,
Tuesday, June 9, 1936, 2 p. m.**

PRESIDING:
Dr. William D. Smith, Boston, Chairman.
Dr. Laurence B. Ellis, Boston, Secretary.

CHAIRMAN SMITH: Will the meeting please come to order.

The first duty of the Section is the selection of the Chairman and the Secretary for the coming year, and, in accordance with the usual custom, the Chair will appoint as the Nominating Committee to suggest names Dr. Dwight O'Hara, Chairman, Dr. George R. Minot and Dr. Chester M. Jones. They will report later and abide the pleasure of the Section.

I do not see Dr. Hamilton here. Apparently she is delayed, so we will pass on to the second paper. To those of us who have had our moments of indecision whether to transfuse or not to transfuse in some of our medical problems, Dr. Bock's paper should be of interest. His subject is "The Use and Abuse of Blood Transfusions."

THE USE AND ABUSE OF BLOOD TRANSFUSIONS*

BY ARLIE V. BOCK, M.D.†

THE mass of literature on the subject of blood transfusions accumulated during the past twenty-five years is so great and most of it so readily available that one shows lack of temerity at least to attempt a discussion of the subject before this audience. The transfusion of blood may be a life-saving procedure under certain circumstances, it may be a necessary supportive measure under others, but it is too often undertaken when the doctor can think of nothing else to do after all other therapy has failed. My objective today is to discuss briefly the common surgical and medical conditions for which transfusion of blood is indicated, in which we can expect good physiological results, and to point out those conditions in which it is little more than a gesture, done, as it were, to satisfy the urge to do something.

SURGICAL INDICATIONS

1. *Shock.* Many theories of the cause of primary and secondary shock have been offered by able investigators, most of them recently reviewed briefly by Blalock.[1] Because of the complexity of the events no theory yet proposed can be considered the final answer as to the etiology of shock. We know that if treatment of the condition is to be successful it must accomplish two things, restoration of diminished blood volume and elevation of low blood pressure. Blood volume may be reduced by gross hemorrhage or it may be reduced by blood lost in the periphery of the body, as suggested by Freeman,[2] or by extravasation of serum through damaged capillaries. If hemorrhage has occurred, transfusion of blood, together with such supportive measures as heat, is the immediate indication. No other therapy is so successful. In shock without much or any hemorrhage, 6 per cent gum acacia in normal saline may be just as effective as blood, and has the advantage of greater availability. Repeated transfusions of blood or infusions of acacia may be necessary but, are usually not, if no delay has occurred in the first instance. Acacia may be used as a supportive measure until transfusion can be arranged. Prolongation of the shock state results in tissue asphyxia, capillary damage, petechial hemorrhages, and rapid change in general to an irreversible state.

One of the common accompaniments of shock is dehydration, a state associated with loss of water, base, chloride and increase of nonprotein nitrogen. When such a state exists, transfusion alone is not adequate therapy but normal salt solution, often in large quantities, should be administered intravenously, or it may be given in eight-ounce quantities by rectum every half hour. When facilities permit, serum chloride

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determinations form a useful guide as to the amount of salt required.

2. *Hemorrhage.* The use for transfusion following hemorrhage is obvious but one important phenomenon has not received the attention which it merits. During the war Robertson and I[3] repeatedly observed the fact that following hemorrhage the systolic blood pressure might be held for relatively long periods at levels of 125 to 140 mm., accompanied by a rapid pulse. This finding at first gave us a sense of security. After a few hours such a patient might be found in shock. There appeared to be little doubt that a widespread peripheral vasoconstriction had sustained a normal or somewhat elevated level of blood pressure and that shock appeared upon failure of this mechanism. Now, Freeman[4] believes that tissue asphyxia under these circumstances ultimately causes the breakdown of the vasoconstrictor system, with resulting fall in blood pressure and precipitation of shock. He has made similar observations concerning the blood pressure reactions in the attempt of the body to maintain the circulation.

In civil practice the above mechanism is seen most often following hemorrhage from duodenal ulcer. If the hemorrhage is severe, with rapid fall of hemoglobin to 50 or below, with pulse rate 120 or more, even though the blood pressure may remain at a normal level, transfusion should be undertaken without delay. This therapy is often not done on the ground that transfusion will raise the blood pressure and thus inducе more hemorrhage. This fallacy is one of the most persistent in the medicine of today. It arises from false reasoning, or the lack of reasoning, rather than from direct observation of events. If blood pressure is low in these circumstances transfusion tends to restore a normal level; if the blood pressure remains at a normal level or is raised somewhat above normal, transfusion of 500 cc. or more of blood will not cause an increase in blood pressure. Furthermore, the introduction of normal blood is the most effective method, short of ligature of the bleeding vessel, that we possess to insure cessation of hemorrhage by establishing closure of an open vessel through blood clotting. Transfusion of blood may be life-saving under these circumstances. It may be necessary to repeat it several times, especially if the patient is fifty years of age or older, because of sclerosis of the bleeding vessel. Surgery, until the bleeding has been stopped, is notoriously dangerous. After severe hemorrhage from other causes, such as trauma, transfusion of blood may not only prevent shock but will do much to shorten the period of convalescence. Surgeons as a whole would do well by their patients if they knew more about hemoglobin estimations and red cell counts than seems to be the case generally.

3. *Sepsis.* It is possible to waste more blood in the treatment of sepsis than for any other one condition. With the exception of hemolytic streptococcal infections, if the necessary surgery has been accomplished, more can be done for the welfare of the patient by prevention of dehydration through maintenance of normal serum chlorides than by transfusion of blood. Severe anemia due to sepsis is an indication for transfusion, but sepsis per se without evidence of anemia is not an indication for this procedure.

In severe infections with hemolytic streptococcus, Lyons[5] has recently published important data concerning treatment by transfusion. A donor is selected who is found by appropriate tests to have a relatively high titer of antibacterial antibody for the particular hemolytic streptococcus causing the infection. Transfusion with such blood may confer sufficient passive immunity to abort the infection within a few hours. The technic of selecting such a donor can only be carried out by a trained worker so that immunotransfusions of this type, involving a somewhat complicated technic, can only be done where facilities for proper study of the case are available. It would be a matter of chance if transfusion, carried out in the usual way, achieved a notable result.

4. *Other Conditions.* Surgeons are often obliged to transfuse patients suffering from anemia due to cancer, ulcerative colitis, and so forth, before and after surgery is attempted. This is valuable supportive treatment without which many surgical procedures would fail. Obstetrical practice occasionally presents problems in the treatment of toxemias in which the technic of plasmapheresis may play an important rôle. Here the patient is bled, the corpuscles separated from the plasma, washed, and restored to the body in a medium of normal saline or Locke's solution.

MEDICAL CONDITIONS

Before proceeding farther, I should like to discuss for a moment an idea apparently held about transfusion of blood. There is a time-honored fable about overloading the circulation. Because in many conditions for which transfusion is considered the pulse is rapid and feeble and the blood pressure low, the impression may be created that the heart is in a state of partial failure. This notion arises because the condition of the pulse and the state of the blood pressure are relatively objective phenomena, and readily observed. The crying need of the rest of the body is not so easily ascertained. If we could as readily observe the state of the cells of the brain, kidneys, capillaries, endocrine

glands, and so forth, we would think less than we do of overloading the circulation. Every physician dealing with this problem should read Meek and Eyster's[6] paper of 1922 on the effect of plethora on diastolic heart size and output of the heart. They gave intravenous injections of acacia, normal saline, and whole blood to normal dogs in quantities varying from 25 to 103 per cent of the total blood volume without increasing permanently the diastolic size of the heart as demonstrated by x-ray measurements. Hemoglobin estimations indicated that most of the injected fluid was still in the circulation and they demonstrated that capillaries and venules acted as reservoirs for storage of excess fluid. If results like this can be achieved at a time when the vascular bed contains its normal quota of blood, there is little ground for the belief that the circulation will be embarrassed by transfusion at a time when the total circulating volume is decreased.

Another idea about which there seems to be some confusion is the necessity for small blood transfusions, due in part to such considerations as the effect upon blood pressure in the presence of hemorrhage, overloading of the circulation, and in part to the effect upon the bone marrow in producing blood. With reference to effects on the blood pressure and heart, if there is known disease of the heart or if acute pathology of the lungs is present, the transfusion of citrated blood is the method of election since due time can be taken for the injection of relatively large quantities of blood. The hasty injection of blood by the paraffine tube method may produce ill-effects in the face of diseased heart or lungs. With reference to the effect of transfusion upon the bone marrow there is a notion that small transfusions stimulate bone marrow activity and large transfusions depress this function. I know of no data in man to support either of these contentions. In dogs, aplasia may result from repeated transfusions. Small transfusions are apparently of use in the rare severe cases of icterus neonatorum, and in two other conditions, purpura hemorrhagica and hemophilia, to be mentioned later.

There is no risk of transfusion, as Minot has pointed out, comparable with that involved in the administration of incompatible blood. Proper matching of the blood of recipient and donor must not be neglected. Careless technic also is responsible for many bad results.

The following medical conditions may require treatment by blood transfusions:

1. *Gastrointestinal Hemorrhage.* Severe bleeding such as may occur from duodenal ulcer may present an emergency the treatment of which requires experience and knowledge of physiologic effects produced by hemorrhage. The general condition of the patient and the pulse rate must be watched closely. The indications for transfusion are discussed above.

2. *Secondary Anemia.* There are many cases of secondary anemia due to chronic blood loss. In this category may be mentioned cases of uterine bleeding, bleeding from diaphragmatic hernia, duodenal ulcer and hemorrhoids. Occasionally transfusion may be necessary in such instances but usually care as to diet and the administration of adequate amounts of iron, such as ferrous sulphate, 12-24 grains daily, constitute good therapy when the bleeding has been stopped. The anemia of pregnancy and nutritional anemia usually respond to the latter therapy also.

3. *Hemophilia.* In many cases of hemorrhage, due to the nature of this disease, transfusion of blood may be necessary to stop bleeding. Patek and Stetson[7] have recently shown that the coagulation time of hemophilic blood can be effectively reduced by the injection of relatively small quantities of blood, 100-200 cc. The duration of the effect is shorter than when larger quantities of blood are given. They suggest, in the face of persistent hemorrhage, giving a transfusion of 500 cc. or more and following this with small transfusions every second day or so until healing of the site of hemorrhage has advanced to a safe state.

4. *Purpura Hemorrhagica.* There is good evidence that transfused blood acts almost as a specific in controlling this affection. There are certain acute cases and some chronic cases in which splenectomy may be necessary but this step should not usually be taken unless repeated transfusions have failed. Jones and Tocantins[8] have shown that small frequently repeated transfusions give more favorable results than may be obtained by large transfusions. They use amounts up to 300 cc. We do not know the cause of this disease or why the administration of blood has such favorable action.

5. *Pernicious Anemia.* Since the advent of liver therapy the idea has become prevalent that transfusion is a menace rather than a help in pernicious anemia. It is true that liver therapy has removed the former necessity of blood transfusion in most of these cases. Transfusion of blood, however, is still the first line of defence in those cases exhibiting an acute psychosis or which may be on the verge of this state, and in cases in a moribund state with or without evidences of congestive failure. Transfusion may of course fail to save extreme cases, but the presence of pulmonary râles, low blood pressure, and so forth should not deter us from transfusing a large amount of blood slowly by the citrate method. The shock-like state of such patients is a direct result of prolonged anoxemia and cannot often be corrected except

by immediately increasing the oxygen-carrying capacity of the blood.

6. *Chronic Benzol Poisoning.* Long exposure to benzol in susceptible cases may produce a severe aplastic state of the bone marrow, accompanied, of course, by grave anemia. Repeated transfusions carried on for months, and in some instances years, are the only known therapy.

7. *Low Serum Protein.* In cases of nephrosis, nutritional anemia and acute yellow atrophy frequent attempts have been made to increase low levels of serum protein by transfusion. In rare cases, successful results have been obtained but for the most part the therapy offered by blood transfusions appears to be useless. The constant loss of protein through the kidneys in nephrosis may be a factor. In nutritional anemia no such external loss of protein occurs, but the failure to raise serum protein by transfusion is about as notable as in nephrosis. A more logical mode of attack seems to be the feeding of proper proteins as suggested by the work of Pommerenke, Slavin, Kariher and Whipple.[9]

8. *Medical Shock.* There is a variety of medical conditions which produces a state of shock, such as diabetic coma, collapse in lobar pneumonia, and infarction of the heart incident to coronary thrombosis, in the treatment of which transfusion may occasionally be necessary, but the major therapy lies in the direction of replacing salt loss and water loss. Other therapy is often indicated but, unless the electrolyte and water balances are restored, success is not likely to be attained. The picture of cardiac failure so often present prevents many physicians from applying the use of saline solutions, but I suggest to them a trial of such simple measures. The use of salt as such and of normal saline in the routine treatment of lobar pneumonia, for example, ranks with good nursing care in my judgment. Atchley[10] has recently given an excellent review of the problem in general.

9. *Miscellaneous Conditions.* The transfusion of blood has a place in the preoperative preparation of long-standing cases of obstructive jaundice. It is often necessary in cases of bleeding due to cirrhosis and Banti's Disease, in severe cases of hemolytic anemia, acute yellow atrophy, aniline and other poisonings. There are not infrequently cases of chronic anemia of unknown etiology not benefited greatly by any therapy except transfusion of blood which may have to be done repeatedly over many months.

THE ABUSE OF TRANSFUSION

Physicians as a whole possess an admirable trait in manifesting a desire to leave no stone unturned in the general care of patients. The sense of responsibility we feel not infrequently leads us into a morass, retreat from which may be painful to say the least. A typical instance of this is represented by a lesson difficult to learn, that is the use of blood transfusion in the type of case we call, for the want of a better name, acute leukemia. Once the diagnosis is made, the family should be informed of the inevitable outcome, and, if the subject of transfusion is brought up, they should be advised against it. If transfusions are attempted, one of two things generally happens, either a severe fatal transfusion reaction occurs or life may be miserably prolonged for a few weeks. In chronic leukemia, there may be occasional circumstances justifying transfusion but usually there appears to be little justification for the procedure.

The anemia of Hodgkin's disease (malignant lymphoma) is not an indication for transfusion since the presence of the anemia is evidence of the terminal state. The impulse to transfuse these cases springs from hope eternal but has no rational basis unless there is some extraordinary reason for attempting to postpone the end.

The same remarks apply to the problem of transfusing cases of chronic nephritis, of malignant hypertension and other conditions. Patients are also being transfused because of weakness and debility due to various causes with results seldom worth the effort. As a ship needs a rudder, the doctor needs to know the reason why before he attempts such a major therapeutic effort.

In conclusion, it seems clear that transfusion of blood is a useful method of therapy in combating medical and surgical shock, in treating cases of severe hemorrhage and in cases of secondary anemia in which the cause is due to blood loss. The procedure should be used as a preoperative and postoperative measure in cases exhibiting anemia such as may occur in cancer, ulcerative colitis, uterine bleeding and sepsis. Immunotransfusions in hemolytic streptococcus infections appear to have a promising future. Transfused blood has a specific action in stopping bleeding due to hemophilia and apparently also in purpura hemorrhagica. Repeated transfusions may tide over cases of chronic benzol poisoning until the bone marrow becomes competent. Except in pernicious anemia, and then only under special circumstances, there is little use for transfusion in primary blood diseases.

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CHAIRMAN SMITH: I have a plea from the extreme rear of the hall that the speakers should try to speak directly into the microphone. Someone suggests that if they will put their arm about it as they read their papers, no one will miss any features of the talk.

The discussion of this paper will be opened by Dr. George R. Minot of Boston.

DR. GEORGE R. MINOT, Boston: When Richard Lower wrote his paper describing his famous experiments on transfusing blood from one animal to another in February, 1665, he entitled the communication, "A Method of Transfusing Blood." He paid detailed attention to technic. That aspect of transfusion must not be forgotten. I will not review that topic but wish to stress the importance, in performing citrate transfusions, of using strictly freshly distilled water, distilled in hard glass not soft glass or metal stills. Attention to this matter will aid in preventing certain common reactions, as will attention to the type of rubber connections used and chemical cleanliness.

The donor, of course, must be healthy and selected by carefully performed "agglutination tests". It is wise to select one who is subject to no allergic condition and who has not eaten for six hours. Even with all precautions taken, reactions that are not well understood occur in severely anemic patients. They resemble circulatory failure or shock, and develop one to twenty-four hours after transfusion. It is this type of reaction that makes it desirable to try to avoid transfusion in cases of chronic severe anemia, like pernicious anemia, where "liver extract" rather than blood is almost always the primary need. However, in severe anemia of deficient states, like pernicious anemia, if, when the patient is at complete rest in bed, distinct clinical signs of insufficient oxygen carriage are present, transfusion is wise. If the patient has a cardiac lesion, such symptoms may occur when there is a relatively high level of hemoglobin; and anginal symptoms and those of congestive failure when associated with insufficient hemoglobin for the given demands may diminish greatly following transfusion. It is better to avoid transfusion unless such symptoms are very pronounced. Reflection indicates that transfusion is rarely needed in pernicious anemia, since clinical improvement occurs within a few days after adequate liver therapy.

Since the regular use of blood to cure hemorrhagic disease of the new-born, few infants die of this condition in contrast to over 80 per cent about thirty-five years ago. In other hemorrhagic conditions the benefit of transfusion is largely passive and usually the effect lasts but a few days. What we need for hemophilia is material to meet with regularity the deficiency of the clotting mechanism. The work of McKhann and Eley, which shows that the distinct value of a placental extract has great promise, and Patek's and Stetson's observations bear on the problem.

In leukemia, as in other fatal diseases, transfusion may keep the patient alive until the diagnosis is established and serve to check disagreeable hemorrhagic manifestations. It may enable some of these patients to lead a more comfortable existence when otherwise they would be confined to bed. Often the decision regarding transfusion in leukemia depends on the demands of the family and becomes a problem of ethics and morals.

The use of transfusion in the different varieties of idiopathic chronic aplastic anemia with not only physiologic aplasia, but also partial anatomic aplasia, is comparable with the use of transfusion in pernicious anemia before the days of liver therapy. It can act to keep the patient on his feet, perhaps actually initiate a remission, and it has led with repetition at varying intervals to some of these individuals maintaining a useful life for often three, and even over eight, years.

The chief value of transfusion of blood is found in its immediate effects in increasing blood volume, hemoglobin concentration, and factors concerned with the coagulation of the blood; and if donors are properly selected in combating certain types of streptococcus infection.

CHAIRMAN SMITH: The subject is now open for discussion from the floor, but the Chair will have to ask each discusser to come to the platform. Otherwise he will hardly be heard. We will also ask the discussers to give their names and addresses to the stenographer before beginning to talk.

If there is no discussion from the floor, we will go on with the next paper. We are fortunate in having here this afternoon an authority on a subject of constantly increasing interest, that is, industrial hazards. The next paper will be "Some New and Unfamiliar Industrial Poisons" by Dr. Alice Hamilton, Assistant Professor of Industrial Medicine, Emeritus, Harvard Medical School. Dr. Hamilton.

SOME NEW AND UNFAMILIAR INDUSTRIAL POISONS*

BY ALICE HAMILTON, M.D.†

THE title of this paper is, in a way, incorrect, for several of the substances that will be considered have been known to be poisonous for many years. Their increased use in industry, however, has placed them in the group of industrial poisons and has brought to light new and unfamiliar effects.

The poisons I will discuss briefly are certain chlorinated hydrocarbons widely used as degreasers, dry cleansers, solvents for rubber, gums, resins, waxes, thinners for coatings of many kinds; also an old poison, carbon disulphide, which is now very important and has revealed an amazingly complex nature; and finally, a number of compounds which have apparently damaging effects of various kinds on the blood. In connection with all these our

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knowledge is still very incomplete; it is like a picture puzzle which has been put together only in spots. The spots are clear and distinct but we have no idea what the many empty spaces should contain.

Carbon disulphide is not a new poison. It is one of the oldest industrial poisons but I find that in this country it is almost unknown. Not long ago, having heard from a young medical graduate of a number of cases of psychoses of various kinds which had occurred recently in men and women employed in a large artificial silk factory, I wrote to one of the physicians in charge of the nearest state asylum for the insane asking him if he had reason to believe that any of the cases of insanity committed to the asylum from that town were caused by exposure to carbon disulphide. He wrote back in answer that he had never heard of carbon disulphide in the rayon industry and had no idea what its poisonous action would be. A few years before this I had had a long telegram from another state signed by an industrial nurse which informed me that an epidemic of insanity had broken out in a rayon factory and the doctors wanted to know what it meant.

It happens that both these plants are situated in states which have no occupational disease compensation, the employer escapes all expense for such cases unless, as rarely happens, suit for damage is brought in a civil court. In these states it is still possible to cover with a mantle of almost complete secrecy unpleasant features of industry and I have never been able to follow up the interesting beginnings of these two stories. I do know, however, from experience in more advanced states, that carbon disulphide poisoning in rayon manufacture means inexcusable negligence.

Carbon disulphide came into prominence with the rubber industry and the literature concerning its toxic action began in 1851, ran through the 80's and 90's up to 1905, then there was an interval which represents safer practices in rubber manufacture; and then suddenly, in quite recent years, a flood of medical reports has come from France, Italy, Holland, Germany and Japan telling of cases of intoxication from its use in that new and growing industry, the making of artificial silk.

Rubber, to make it usable, must be vulcanized which means that sulphur must be incorporated with it and there are two ways of effecting this, either to introduce flowers of sulphur with heat and pressure or to use sulphur monochloride with carbon disulphide, dipping the goods in the mixture or hanging them in the vapors. On the Continent and in England in the early days, the latter method was largely used and it was carbon disulphide that gave the rubber industry a place among the dangerous trades. In this country, heat vulcanization has been the method preferred and, although up to some fifteen years ago it was still possible to find the so-called "acid cure" in use, nowadays carbon disulphide has practically disappeared from American rubber manufacture; and, far from being a dangerous trade, the records of our great rubber city, Akron, Ohio, show that it can be made one of the least harmful to the health of the workers.

But when carbon disulphide disappeared from rubber factories it came into sudden prominence in a new industry. Artificial silk is produced in various ways, only one of which requires this reagent; but, unfortunately, the one which does is most widely used all over the world, namely, the rayon process. Cellulose, after treatment with strong caustic alkaline solution, is placed in a great revolving cylinder with carbon disulphide which changes it to cellulose xanthate, a yellow rubbery mass. It is quite possible to carry on this reaction and to handle the resulting xanthate without exposing workers to the poison, as I have seen done in well-managed factories; but the reports that come to us from abroad and the vague rumors from some of our states show that factory hygiene is faulty in many cases.

Carbon disulphide is a specific poison to the central nervous system, a severe generalized nerve poison. The chronic form, which alone is important in industry, is characterized by paralyses and psychoses of various kinds and a typical toxic amblyopia. Much careful work was done in this field by the Germans some thirty years ago and the physician interested in the subject is referred to the articles by Quensel,[1] by Laudenheimer[2] (who analyzed fifty cases of insanity and paralysis in Flechsig's clinic in Leipzig) and by Köster[3] who asserts that carbon disulphide is as variable in its action on the central nervous system as alcohol or lead. The most usual form of insanity is the manic-depressive type, which lasts for some months or a year or two, then usually clears up but in rarer instances passes into lasting dementia. The paralysis is usually motor, affecting chiefly the peroneal muscles and the extensors of the forearms. In some cases there are coarse jerking movements, muscular contractures or tabes-like ataxia. Recovery is fairly rapid if the exposure ceases. Dimness of vision is a common symptom and, according to Birch-Hirschfeld (see Köster), the lesion caused by carbon disulphide is like that caused by lead and by alcohol, a retrobulbar neuritis with atrophy of the optic nerve.

The latest studies of carbon disulphide poisoning come to us from Italy and France. The histories show retrobulbar neuritis, sometimes transient, sometimes resulting in permanent loss of visual acuity.[4] Paralyses of various kinds are reported, the most interesting of which is a

form of Parkinson's disease of which several instances have occurred in Italy and are assumed to point to a lesion in the globus pallidus of the corpus striatum.[5, 6] The tremor is like that of paralysis agitans. Polyneuritis, affecting the nerves of the lower extremities, has been described also and sexual impotence is a very common symptom in men. Ranelletti[7] analyzed one hundred histories of carbon disulphide poisoning, seventy-seven of them from the artificial silk industry, and found eighty with involvement of the central nervous system, fifty-two of these with mental derangement, mainly of a maniacal type, with delirium or hallucinations, but a few instances of dementia. The attack usually began, after an exposure of some months or even years, with depression, rarely with sudden excitement and hallucinations. I have seen an instance of each of these forms of onset. The paralysis affected the motor fibres more than the sensory although in ten instances there were neuritic pains. Ranelletti found that recovery was surprisingly rapid except in cases of dementia.

The morphologic changes of the central nervous system consist in fatty degeneration of the ganglion cells which has been observed in the cerebral cortex, the gray matter of the cord, the spinal ganglia and recently in the basal ganglia of the brain.[7]

In view of the wide distribution of rayon manufacture in this country and the general ignorance concerning its dangers, we must conclude that here is an important subject for study by the toxicologist, the psychiatrist and the industrial physician.

Carbon tetrachloride has been thoroughly studied by pharmacologists in connection with its use as an anthelmintic and our experience with industrial intoxication from the fumes of this compound has in most respects confirmed the laboratory findings. Thus MacMahon and Weiss[8] found in a human victim in the blood of the large pulmonary arteries and the right side of the heart 60 per cent of fat, a condition which Rosenthal and Lillie,[9] had produced in dogs; Butsch[10] had a case of industrial poisoning with symptoms simulating portal cirrhosis, such as Bollman and Mann[11] had found in dogs; and Ravina[12] used Minot and Cutler's discovery that the severity of carbon tetrachloride poisoning is increased by a negative calcium balance,[13] in treating successfully cases of intoxication in man. In both human and animal poisoning, alcohol has a markedly favoring influence.

However, it is well to remember that human poisoning differs from experimental poisoning in animals in some respects. In the latter, it is the damage to the liver that dominates the picture, the kidneys are much less involved. In man, although there is at first severe vomiting, intestinal pain, diarrhea, jaundice and tenderness over the liver, and an excess of blood urea and diminished excretion of urine that may also be traced to liver damage, still, in fatal cases there is evidence of profound involvement of the kidneys, increasing oliguria, generalized edema, finally complete anuria and uremic convulsions.

A rare feature of this form of industrial intoxication is an involvement of the optic nerve with visual disturbances resembling those caused by carbon disulphide, namely, bilateral, peripheral narrowing of the visual fields. Five such cases were recently reported by Wirtschafter.[14]

Carbon tetrachloride is a very important element in industry because it is noninflammable and it is an excellent solvent for fats and gums, natural and synthetic. It is also volatile. These last two properties, that it volatilizes rapidly and has a strong affinity for fats, explain its danger to the worker.

Ethylene dichloride is a newer solvent belonging to this class; the proper chemical name is dichlorethane. It is the solvent most used in making photographic films; it is beginning to be used as a degreaser in laundries and in the dope used for coating the interior of beer vats. This last job, which is obviously dangerous if a toxic solvent is used, gave rise to very distressing cases of methyl alcohol poisoning with blindness and sometimes death in the period before prohibition when beer vats were lined with shellac dissolved in wood alcohol. The widespread poisoning from drinking methyl alcohol in the early years of prohibition gave the public an even exaggerated fear of this solvent and nowadays one rarely finds it in use without great precautions to protect the worker. However, the lining of beer vats has not lost its danger. Recently two men engaged in this work were overcome by the fumes of ethylene dichloride, one dying some hours later. The autopsy showed excess of fat in the blood, and suggested the possibility that fat embolism rather than asphyxiation was the cause of death.

Another beer-vat fatality was unofficially reported not long ago, but here the solvent used in the lining coat was not ethylene dichloride but trichlorethylene. This compound has come into use not only as a solvent for coatings but for all the uses to which carbon tetrachloride has for many years been put. It appears to be a more powerful narcotic than the latter and the cases reported from industry are numerous but, for the most part, not serious, revealing no such organic damage as occurs from the older poison. Stüber,[15] has collected no less than 284 cases, chiefly from German sources, some from English and Austrian, none from this country. Most of these were cases of acute narcosis,

rarely severe, and fatal only if the victim could not be rescued in time—an accident which has happened in this country as well. Included in this list are cases which must be regarded as dubious for the lesions cannot be produced in animals, nor are they observed in man when pure trichlorethylene is used therapeutically in the treatment of facial neuralgia.

This form of treatment, it will be remembered, was based on the report made in 1916 by Plessner,[16] of four cases of a very unusual form of industrial intoxication which came on after a few hours' exposure to what was supposed to be trichlorethylene. The first symptom was a slight transient narcosis, followed by numbness of the lining of the mouth and of the nose and of the skin of the face with impairment of the sense of taste and of smell. The numbness was bilateral in three of the four cases and two of these three also had impairment of vision with some pallor and edema of the papilla. None of them developed keratitis neuroparalytica, but trophic changes were seen in one man who lost all his teeth. Seven months later Plessner found that the paralysis of the sensory fibres of the trigeminus was still complete. It was on the basis of these cases that Oppenheim recommended the use of trichlorethylene as a remedy for the pain of facial neuralgia and I am told that it is still used for this purpose in our country although, according to the Germans, it does not produce anesthesia of the skin and acts simply as a general narcotic.

The suspicion is strong that Plessner's cases suffered a mixed intoxication, trichlorethylene playing a minor part. In the first place it had been used in that plant for some months without any complaint, then suddenly five men—one was discovered later—developed serious symptoms after only a day's exposure to the fumes. It happened during the war when German manufacturers were forced to use all sorts of substitutes and rarely knew just what they were using. But the researches of Kalinowsky[17] eleven years later weigh even more strongly against the theory that trichlorethylene was responsible for the trigeminal paralysis of Plessner. Kalinowsky saw two cases practically identical with these (bilateral sensory paralysis, loss of teeth) in men exposed to fumes containing some chlorinated hydrocarbons but not di- or tri- or tetrachlorethylene. This led him to trace Plessner's patients (Plessner had died in the interval) but he found only one still living, the man who had been least affected, with sensory paralysis of one side only, which was still present. This man had suffered a stroke of apoplexy from which he had recovered but the others had died, apparently from apoplexy. Kalinowsky was told of a fifth man whom Plessner did not see, a man who worked only two days in the fumes, then became very ill and died of what was called "a stroke". These occurrences can hardly be explained as pure coincidences, but neither can they be attributed to the unaided action of trichlorethylene.

It is true that other instances of paralysis of the sensory branches of the trigeminus have followed exposure to trichlorethylene in industry, Stüber collected four instances, and Baader[18] has seen a case of retrobulbar neuritis and one of optic atrophy following long exposure to this solvent. An American case of retrobulbar neuritis following fourteen months' exposure has been reported to me recently. But in none of these instances is there proof that the compound used was chemically pure and in industry it is not necessary that it should be pure. When it is chemically pure as in therapeutic use, no lasting injury to either the trigeminus or the optic nerve has ever been observed. This is made clear in an article in the *Journal of the American Medical Association* of a few weeks back, in which Eichert,[19] after reviewing the literature of supposed poisoning from this compound, says that he has been able to discover only one nonindustrial case of a toxic syndrome following a prolonged and excessive use of trichlorethylene as a therapeutic agent. He adds two cases of his own, but in none of these three was there any anesthesia of the area innervated by the trigeminal nerve, or evidence of injury to the optic nerve.

One thing, however, must not be forgotten, that clinical and industrial poisoning are not the same, that the lesions caused by prolonged absorption of small doses do not usually appear when large doses are administered at rare intervals. Both lead and benzol are striking examples of the greater damage done by the slow method as compared with the rapid.

In connection with both carbon tetrachloride and trichlorethylene there is a question still unsettled that is very important especially as it comes up in compensation claims. It has to do with the occurrence of bronchial pneumonia or acute pulmonary congestion with edema as a sequel to intoxication from these fumes. In view of the fact that acute pulmonary inflammation sometimes follows surgical anesthesia with chloroform, it seems reasonable to accept as instances of the action of these compounds so closely related to chloroform cases of pneumonia which develop after a severe acute narcosis. One such case in which the bronchopneumonia followed the inhaling of vomitus (see Stüber) is certainly beyond argument and the one described by Koch[20] in which the victim died of severe narcosis and the whole respiratory tract was found in a state of acute

inflammation, seems also beyond doubt. But much more numerous are the cases of bronchopneumonia in men who have inhaled smaller doses over a long period, who have never been narcotized. About such cases, we find it impossible as yet to speak positively, that is, with the degree of certainty which is necessary before a compensation board.

As clinicians you have all doubtless been interested in the researches in various new forms of apparently primary blood disease, the anemias and leukemias which we call idiopathic in the sense that their cause is as yet undiscovered. The literature of Schultz's agranulocytic angina is already very voluminous and includes such a variety of pictures that it is now no longer regarded as a clinical entity and while in some instances a bacterial agent seems to be the exciting cause, in others the suppurative lesions are apparently only a secondary feature, and of late the action of some drug is suspected. In connection with the last, we are all familiar with the cases of aplastic anemia which followed Koranyi's treatment of leukemia with benzol and those reported from time to time as following treatment with salvarsan and neoarsphenamine. More recently amidopyrine-barbiturate compounds have been accused of causing agranulocytosis and Schustrow and Salistowskaja[27] have reported three cases with two deaths which were attributed to alphadinitrophenol, recently introduced for the treatment of obesity.

Now here is another large and interesting field which awaits the student of industrial diseases, a field largely unexplored as yet, with the exception of benzol, and even there the cases actually studied are few, not half so numerous as the cases of agranulocytic angina, although Schultz's first article appeared only fourteen years ago. Diseases of the blood in industrial workers are classed as idiopathic always, unless benzol can be incriminated and even then, if the clinical and histologic picture differs at all from the accepted standard of typical aplastic anemia. Yet we are ready enough to admit variations in the blood findings and presence or absence of hemorrhage and of suppurative lesions in nonindustrial cases, attributing such variations to the degree of marrow injury and the particular elements of the marrow most affected.

There are several toxic compounds of more or less importance in industry which have been studied with sufficient care to enable us to speak with certainty of their probable action. Alphadinitrophenol is one, for it is an essential ingredient of the French explosive, mélinite, and during the war we learned enough of its character to be amazed and alarmed when we found it was being recommended as a safe remedy for obesity. Two other compounds of this same group, nitro derivatives of the benzene ring, were also studied exhaustively during the war, trinitrotoluene and dinitrobenzene, both of which are capable of severely damaging the bone marrow. These three are used in industry in the production of dyes and drugs and so is a whole series of related compounds about which we know less, the nitranilins and chloranilins, the chlor- and chlornitrobenzenes, the toluidins, the chlortoluidins and the diamines, acetanilid, all of them important intermediates and all producing blood changes which by some are said to consist chiefly in the formation of methemoglobin, by others in destruction of red blood cells with slow regeneration, by others in actual hemolysis like that caused by arsine.

Tetrachlorethane was a war poison of great importance, for it was the solvent best adapted for use in airplane dope. Before it was abandoned by the Germans and the British on account of its toxic nature, it had caused in both countries a number of cases of fatal acute yellow atrophy of the liver.[22, 23] In British factory inspection reports such cases are listed under "toxic jaundice", together with poisoning from arsine. Tetrachlorethane also proved to be destructive to the blood-forming tissues of the bone marrow and instances of typical aplastic anemia occurred. In this country this solvent was for a while used in the making of artificial silk and Minot and Smith[24] were able to detect in the blood of workers exposed to the fumes an early change which served to give warning of danger. This was the appearance of a relatively large number of leucocytes of the endothelial type, up to some 40 per cent, and in some instances these would show degenerative changes.

Trinitrotoluene is another of the benzene derivatives which was found during the war to exert, in exceptional cases, the action typical of benzene, the victims developing aplastic anemia, granulocytopenia and thrombopenia. Kegel and his colleagues[25] found that the cases of poisoning from methyl chloride fumes, in the famous mass poisoning in Chicago, showed in their blood during the first week, findings typical of aplastic anemia.

There are many as yet unsolved problems in this field. Benzene has been assumed to exert one action only, a destruction of the elements of the bone marrow concerned in the production of erythrocytes, granulocytes, and thrombocytes. But, aside from reports of benzene workers whose blood shows a stage of marrow irritation, we have now several instances of blood pictures diverging widely from the accepted standard, such as anemia with active regeneration and even leukemia. (See Andersen.[26])

Still more obscure is the question whether petroleum benzine—as distinguished from coal tar—or naphtha or gasoline, has any destruc-

tive action on the blood-forming tissues. Cases come to our attention from time to time of profound secondary anemia or primary anemia with purpura hemorrhagica or of some variety of leukemia in men who have been exposed for long periods to fumes of petroleum distillates, but, in the present state of our knowledge, we cannot pronounce them to be of industrial origin. And yet Russian experimenters have produced hemolytic anemia of the aplastic type with leukopenia affecting all classes of leukocytes by exposing animals to fumes of naphtha.[27] Smithies of Chicago[28] published histories of four cases and wrote me of two more in which laking of the blood was a prominent feature and in all these there had been exposure to very volatile oil distillates. As for the relation between leukemia and exposure to petroleum fumes, it may be fantastic, and yet we know that certain petroleum and coal-tar derivatives are capable of setting up carcinomatous changes in the skin. Industrial skin cancer from certain oils and tars is far from uncommon. On the theory that leukemia is a cancer of the blood might we not assume, as a working hypothesis, that the carcinogenetic agent in some cases is a volatile petroleum product?

Cases of polycythemia of supposedly toxic origin also are sometimes brought to our attention and here again it is impossible to speak positively. We do know that an increase in the red cell count has been observed to be caused by chronic exposure to carbon monoxide and to hydrogen cyanide and has been seen in the early stages of benzene and of anilin intoxication, and it was a striking feature of the blood of girls exposed to ether fumes in the manufacture of smokeless powder during the war.[29] Devoto,[30] in Italy, found polycythemia in two cases of mercurialism and Kilgore[31] saw two striking cases in feather workers handling various dyes. One of these had over 9,000,000 red cells and the other over 12,000,000. The first victim died and the marrow of the long bones was found to be in a state of erythroblastic hyperplasia. Among the dyes that were used was paraphenylendiamine, perhaps the most probable causative agent. All this does suggest that a careful study of cases of so-called polycythemia vera might reveal some toxic agent.

In conclusion, may I beg for a careful, detailed job analysis when the history is taken of a working man or woman who presents a puzzling array of symptoms? It may be that such an analysis will throw light on his or her case and also add a valuable item to our scanty knowledge of industrial poisons.

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CHAIRMAN SMITH: I am sure the Section is grateful to Dr. Hamilton for coming here today and giving us this very splendid paper. The discussion will be opened by Dr. W. Irving Clark of Worcester.

DR. W. IRVING CLARK, Worcester: It is a privilege to hear a paper in an unfamiliar field by such an authority as Dr. Hamilton. The newer industrial poisons are unfamiliar even to one practicing in industry unless they are in use in the factory or factories over which he has supervision. To the general practitioner the opportunity of seeing and treating such cases depends upon the presence of factories or shops in his vicinity in which these chemicals are used. In Massachusetts, which is essentially a manufacturing state, there are probably a large number of possible exposures particularly among the

smaller plants where the care of the workers' health is not in the hands of an industrial physician.

For those physicians working in a community where such exposures are possible, it is important in taking the history of a patient who is a worker to go into some detail as to the exact work he was doing, and to find out from him of any possible exposure, if his symptoms suggest an acute or chronic intoxication. We are fortunate in having in this state a Department of Occupational Hygiene at 23 Joy Street, Boston, where information as to the contents of substances bearing trade names can probably be obtained. The determining of the exact chemical responsible for a patient's symptoms is extremely difficult, especially in cases where the exposure has been to a group of such substances as is frequently the case.

Dr. Hamilton's paper suggests that in addition to a careful industrial history, a routine examination of the blood, urine and nervous system may be decidedly helpful in getting an idea of the type of chronic poisoning which may be present.

In the industry with which I am connected, a few chemical exposures occur, but by very careful protective measures such as hoods, respirators, forced ventilation, and skin protection, there have thus far been no cases of severe intoxication except one case of lead poisoning.

A great danger of acute poisoning is from painting, cleaning or repairing tanks or working in similar poorly ventilated closed spaces where a chemical is used, or has been stored. I saw two cases of mild intoxication, lasting only about half an hour, and having no aftereffects, in men painting the inside of a large tank with asphaltum. Since this experience, which occurred several years ago, no man enters a tank of any kind to do any type of work unless he has on a harness and wears an air mask to which air is pumped from outside.

Dr. Hamilton has not spoken of the danger of nitrous fumes in connection with oxyacetylene or electric welding. This hazard has only recently been recognized. In 1934 Bridge[1] stated that at least seventeen cases of nitrous fume poisoning (one fatal) were reported in England that year as a result of the use of large oxyacetylene burners used to heat heavy steel in a shipbuilding operation, where the work was conducted in a confined space.

In 1935 Titus, Warren, and Drinker[2] studied experimentally the effect of the fumes of electric welding upon animals. "The welding time varied from 2 to 5 hours while the animals were exposed at various stages of the welding operation and at various fume concentrations." The animals were exposed to filtered and unfiltered fumes in order to determine whether the fine metallic particles in the fume or the gases were toxic. "The effects on the lungs were like those found in animals exposed to toxic concentrations of irritating gases," namely, pulmonary edema. "The cause of the pulmonary edema is not the iron oxide fume, but the gases generated by the arc, viz., probably nitrogen peroxide and ozone."

In the same year a case of death from welding a galvanized iron tank in a confined space occurred in Washington, D. C.[3]

Such reports make it obvious that electric welding should not be done in a confined space and that, if this is unavoidable, an air mask provided with a hose to bring clean air to the worker is imperative.

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CHAIRMAN SMITH: Is there further discussion from the floor?

DR. GEORGE L. SCHADT, Springfield: *Mr. Chairman*—We have had a most interesting and worthwhile discussion of a subject that in my opinion at least is certainly one of the most pressing before the medical profession today—the problem concerned with the deleterious effects of the newer solvents as poisons on the human system. Dr. Hamilton deserves the thanks of every doctor within sound of her voice for bringing to us a discussion of the subject this afternoon.

I should like to discuss this paper for a few moments from the viewpoint of the clinical pathologist and of the family doctor, though they do say that there are none of the latter existent in this day and generation, and to consider just what interesting and possibly pathologically dangerous conditions may develop in the human organism following employment in industries of these new-fangled solutions known as solvents.

Many chemical manufacturers are today developing and putting on the market a great diversity of these new solvents, some of them under trade names, many, however, according to their true chemical names. Unfortunately little if anything is known with reference to the effects on the human system of these solvents either by the manufacturing chemist, by the industrialist and by the physician. It would certainly seem to me we should know a great deal more with reference to the potential dangers of many of these solvents before permitting them to be used promiscuously in the various industries. This, in my opinion, is a problem for the general practitioner since the use of these solvents in industry is increasing by leaps and bounds each day. I have seen many individuals, both male and female, who in my opinion were suffering from conditions brought about by prolonged exposure or exposure under certain definite circumstances to some of these solvents. I can recall the death of a young woman within the last few years following prolonged exposure to methanol during a period in which long hours prevailed and in which there was an exceedingly high concentration of the solvent in the room in which she worked.

I should like to ask Dr. Hamilton about one phase of the problem that she did not touch upon—the question of concentration and of temperatures in which workers are exposed to the fumes of these solvents. The young woman mentioned above was, as already stated, exposed to a very high concentration of methanol under very high temperature conditions and death took place approximately twenty-four hours after she had been overcome. In my opinion, this question of concentration and of temperature is most important and one that should be carefully studied.

It is my studied opinion that the general practitioner should give more careful attention to industrial workers, men and women, and especially young women, who come to him complaining of symptoms which are too easily and too apt to be classified as "neurotic". Such symptoms are headache, dizziness, nausea and sleeplessness. Many of these workers also complain of minor kidney disturbances and in practically every instance blood examination demonstrates the presence of secondary anemia. This is an exceedingly important point since I am convinced that, if recognized early, all of these individuals may be relieved of their symptoms and working conditions may be changed for them.

Another important factor is that of age, particularly in the female. We have been impressed with the fact that in young women secondary anemia is very common, if not almost universal, with hemo-

globin ranging from 65 to 70 per cent, red blood cells 3,500,000 and blood platelets very much diminished. With reference to blood platelets, in our experience a decrease is one of the early manifestations of organism reaction to the effects of solvents. The kidney reaction is usually manifested by the presence of albumin in the urine ranging from 10 to 30 milligrams per 100 cubic centimeters. No casts are present as a rule, but occasionally a red blood cell is seen. Dr. Hamilton has already stressed this and we should certainly be very careful with these individuals to include urinalysis and a blood examination—at least a hemoglobin determination and a red blood cell and blood platelet count.

In conclusion may I express the opinion that the average employer does not, as yet, seem to appreciate fully his responsibility to his employees when solvents of one kind or another are used and when the employees are being exposed to their fumes under varying conditions and situations. As stated early in this discussion the manufacturing chemist, the employer and, unfortunately, the doctor know altogether too little with reference to these products, especially with reference to their deleterious effects on the human system.

It has been a great pleasure to me to listen to Dr. Hamilton this afternoon and I do hope that in her closing remarks she will discuss a little more fully the question of concentration values and temperatures and how best to control working conditions with industrial solvents and poisons, thus doing our duty by the workers who ultimately become our patients.

DR. B. T. BURLEY, Worcester: *Mr. Chairman*—Recently I had an experience in the use of trichlorethylene which may be of some interest to the profession in general. A retired physician had been under treatment for trigeminal neuralgia and for mild attacks had resorted to inhalation of trichlorethylene. Recently I had to block a branch of the fifth nerve by alcoholic injection to cut short a severe attack. Though the pain was gone I was informed by the nurse, a few days later, that the patient was insisting on the use of two bottles of trichlorethylene daily to promote rest and sleep.

This was to me a new experience and I should like an opinion from Dr. Hamilton as to the possibility of any habit addiction from this drug.

DR. ALICE HAMILTON: *Mr. Chairman*—With regard to the concentration of fumes, it is impossible to speak positively except in the case of benzol, where extensive tests were made of concentration of fumes in the air in actual factories and where that was matched up with the blood pictures of the people working in those factories. In connection with others, we have the experiments of the Public Health Service; but they have always had to do with measured quantities administered to animals, producing acute symptoms. Such conditions do not concern us much in industry. What we are interested in is chronic poisoning.

I have seen statements as to safe limits of carbon tetrachloride, for instance, that run, I believe, from 100 parts per million to 10,000. I have a poor memory for figures so I would not wish you to rely on those figures, but if anyone really wants to know what is the safe concentration of carbon tetrachloride I should advise him to write to Dr. P. A. Davis of the Goodyear Tire and Rubber Company. His answer will be based on wide personal experience.

As for temperature, of course the higher the temperature the more poison is volatilized and the more deeply one breathes. This increases the amount of poison that is taken up.

The question of the youth of workers is of course important. During the war the experience in every country pointed strongly against the employment of the youthful of both sexes but especially young girls in connection with those poisons that have an action on the blood.

As for the last question, cases of addiction to carbon tetrachloride have been reported several times in Germany and I have heard of a few in this country. Lately there have been German reports of addiction to trichlorethylene. The man comes to work in the morning feeling as if he had been intoxicated the night before and is not able to go to work until he has taken some deep inhalations of carbon tetrachloride or trichlorethylene. The case of Baader's I spoke of, optic atrophy, was a trichlorethylene addict.

CHAIRMAN SMITH: I have here the report of the Nominating Committee, consisting of Dr. O'Hara, Dr. Jones and Dr. Minot. They nominate for Chairman for the coming year Dr. Laurence D. Chapin of Springfield and for Secretary Dr. George D. Henderson of Holyoke. Does anyone wish to make further nominations from the floor? It is moved and seconded that nominations be closed. Does someone wish to make the motion that the Secretary be instructed to cast one ballot for Dr. Laurence D. Chapin as Chairman? It is moved and seconded that the Secretary cast one ballot for Dr. Chapin as Chairman. All those in favor will raise their hands; opposed; it is a vote. Dr. Ellis has cast the ballot, and I declare Dr. Chapin duly elected.

Do I hear a motion that the Secretary be empowered to cast one ballot for Dr. George D. Henderson of Holyoke as Secretary for the ensuing year? It is so moved and seconded. All those in favor will raise their hands; those opposed; it is a vote.

Dr. Chester M. Jones has for several years been doing a very interesting and constructive study on the diseases of the liver in the wards of Massachusetts hospitals. The title of his paper is "Newer Concepts of Liver Disease and Their Relation to Treatment." Dr. Jones.

NEWER CONCEPTS OF LIVER DISEASE*

BY CHESTER M. JONES, M.D.†

THE older concepts of liver disease had to deal with confused and fairly inadequate ideas that were associated with such terms as "torpid liver", "bilious attacks", and the like, terms of the most general nature and with no real clinical meaning. Such an unsatisfactory state arose from the fact that the tremendous factor of safety possessed by the organ prevented any adequate estimation of functional disability. Accurate measurement of the functional capacity of the liver is only possible, even with the most modern methods, when the number of normally functioning cells has been reduced to a minimum, a point reached only in

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serious acute liver injury or in advanced chronic disease. Only at such a time do the hepatic cells fail to meet the metabolic and immunologic needs of the body, and only then do the various functional tests begin to give evidence of measurable hepatic failure. It is still necessary to talk about liver disease in terms that are far from precise, and careful clinical observations still constitute the basis on which most diagnostic and therapeutic decisions must be made. Nevertheless, a fairly clear idea of our present knowledge of liver function will be of real value in properly evaluating a given case, and a brief review of this knowledge will be proper. I should like to stress my conviction again, however, that with rare exceptions, clinical experience and judgments based thereon will continue to be of much greater importance than any laboratory data that can be compiled in almost any given case. In spite of a tremendous amount of painstaking research by numerous investigators, laboratory tests still fail to give information that, as a rule, cannot be gained by the ordinary clinical methods employed in studying sick individuals. Here I should like to suggest a comparison between heart disease and hepatic disorders. It is still true that except in cases where signs of frank cardiac failure exist an exact measure of cardiac disability is impossible, even with the most refined methods. Unless the cardiac reserve has been overstepped, the organ can compensate sufficiently to render so-called scientific measurements of only general value. The same is true for the patient who has disease of the liver but is still not decompensated. The determination of the prognosis in liver disease is still more baffling, and clinical skill and observation are just as valuable in sizing up a given hepatic disorder as they are in properly evaluating cardiac disease. This is particularly true when one speaks in terms of laboratory tests performed as single observations. Only by repeated determinations on a given patient can one obtain comparative data that will enable the physician to determine the progress of a disease with any greater surety than by careful bedside observations. Rarely can diagnosis be made by laboratory data alone and, even in those instances where such diagnosis is made, the possibility of hepatic disorder has been considered or the test or tests would not have been carried out.

What are the functions of the liver that can be measured? I shall discuss only those that seem to possess some practical application to the problem of the sick liver. The best known function is that of glycogen formation or storage. This has been recognized since the time of Claude Bernard and is still the most important single function from the point of view of therapy. To measure the ability of the liver to handle carbohydrate material, various tests have been devised, and of these the glucose tolerance test is probably the most valuable. Normally this sugar is utilized directly or completely by the liver. When there is intrahepatic damage of sufficient degree such is not the case and there is a greater or lesser amount of glucose excreted in the urine. According to the most enthusiastic reports, in obstructive jaundice after ingestion of this sugar small amounts are found in the urine; in severe diffuse toxic damage to the liver much greater amounts are to be found. Were such always the case, the test would indeed be a very valuable one in those cases of undetermined jaundice which are frequently so baffling. Unfortunately the test is not infrequently absolutely misleading and cannot be relied upon as a certain diagnostic procedure. Like the other tests to be discussed, repeated determinations are of value in following the progress of a given case. A slightly different test for measuring the ability of the liver to handle carbohydrate is the insulin-water test of Althausen.

A more obvious laboratory procedure is an attempt to measure the intensity of jaundice. Although the liver has only a moderate part to play in the formation of bile pigment, it has the entire problem of excreting it. Even fairly great variations in clinical jaundice are difficult to measure with the eye. The determination of the icteric index or quantitation of the blood bilirubin by the indirect van den Bergh method offers a fairly accurate method for measuring the depth of jaundice in a given patient. As a diagnostic procedure its value lies in the fact that by its use subclinical icterus can be demonstrated.

Another function of the liver enables it to excrete particulate matter and certain dyes that are brought to it through the blood stream. This excretion capacity, which in large part involves the activity of Kupffer's cells, can be more or less grossly estimated by injecting a dye such as bromsulphalein or rose bengal into a vein, and after half an hour, determining the amount of the dye still retained in the circulation. Under ordinary conditions practically no dye will be retained. In the presence of jaundice not due to increased blood destruction, the dye will be retained in varying amounts depending upon the depth of the jaundice. In this respect, therefore, the dye test parallels the bilirubin determination and is of value only if repeated tests give comparative values for following the progress of a case. In the absence of jaundice there still may be marked dye retention in advanced disease of the liver such as a toxic cirrhosis, and the performance of the test may rarely be of diagnostic value. It also may be of some importance in estimating the operative risk in a given case of jaun-

dice. When the dye retention seems to be out of proportion to the depth of jaundice it is undoubtedly true that surgical interference will be hazardous indeed.

In some way that is not understood, the liver is involved in the metabolism of cholesterol. Undoubtedly the liver treats cholesterol in part as an excretion product and, in the presence of diffuse liver damage and jaundice, the level of cholesterol is high in the plasma. This is of no particular diagnostic importance inasmuch as there are numerous other determinations of less technical difficulty which will provide similar information. An additional fact of interest, however, is that serious hepatic failure is associated with a change in the cholesterol-cholesterol ester ratio. Normally cholesterol esters constitute over fifty per cent of the total cholesterol. In diffuse liver damage, especially when associated with the existence of jaundice, the esters form a much smaller proportion of the total plasma value than normal. The finding of a low cholesterol ester value certainly indicates poor hepatic function, but unless repeated determinations are made the test is of little real diagnostic or prognostic value.

The liver has a very close connection with the normal distribution of water in the body. Under ordinary conditions this is not an apparent function of the organ. When there exists serious hepatic insufficiency, however, either in the acute or chronic forms of the disease, edema and ascites may occur. It has usually been considered that the occurrence of ascites was associated with portal obstruction and this is in part true in the cirrhosis. Ascites may occur in acute liver insufficiency and without any obstruction to the portal flow. As a rule edema is an associated finding under such conditions and is due to a general cellular disturbance, secondary to severe liver disease. The only known laboratory finding that helps us to explain such a phenomenon partially, is the inversion of the albumin-globulin ratio in the plasma, frequently with a lowering of the plasma protein.

With such a change in the osmotic pressure relationships in the blood, a movement of water into the tissues and serous cavities is a natural consequence. Additional factors favoring the production of edema are the possible increase in capillary permeability in liver disease and the deglycogenization of the liver itself. Adequate tests to measure accurately this control of the fluid movement in the body do not exist. A simple but approximate method exists, nevertheless, and I am going to emphasize it because of its simplicity. I refer to the measurement of fluid intake and urine output. Such measurements are obviously only moderately accurate as they are usually made by the average nurse or family. By a little insistence, however, a satisfactory idea can be obtained of urinary activity as related to fluid intake. In patients who are seriously ill from hepatic failure one almost invariably finds an associated oliguria. The moment the balance swings toward a return to compensation in liver function the urinary output increases in amount and an obvious diuresis sets in. At times this diuresis is very striking, even in the absence of demonstrable edema or ascites. When it occurs it is extremely rare for the patient's symptoms not to improve, and for recovery not to take place. Because of the ease with which such observations can be made and because of the almost invariable favorable response when such a spontaneous diuresis occurs, I wish to urge the importance of making these determinations in cases of hepatic failure. In my experience they offer the simplest and best means of arriving at a prognosis in many cases.

Several other laboratory tests should be mentioned. Measurement of the serum phosphatase, as suggested by Ivy and others, is said to be of diagnostic value in differentiating the jaundice due to a mechanical block of the common duct and that due to intrahepatic disease of a toxic or infectious origin. In the former there seems to be little if any elevation of the serum phosphatase; in the latter the values reach rather high levels. If this is true, the performance of such a test may well justify itself in these very different groups. The Takata-Ara test is one that has occasioned much comment in recent years. Essentially it is a flocculation test performed on the blood plasma with solutions of sodium carbonate and corrosive sublimate. It probably depends upon the already mentioned albumin-globulin changes in the blood for its findings. When positive it usually means advanced liver disease and it usually is positive in the Laennec type of cirrhosis. As a diagnostic procedure it is usually confirmatory only. Another method of diagnosing the presence of a portal type of cirrhosis is of more importance because of its clinical significance. I refer to the demonstration of esophageal varices by relief films of the esophagus. The obvious reason for making such an examination is usually the occurrence of an unexplained hematemesis. At times, however, portal cirrhosis may be present without any history of bloody vomit and varices may be demonstrated. When found they offer absolute proof of the diagnosis. In addition to its diagnostic significance it is also true that such a finding should be sufficient reason for giving a rather guarded prognosis.

Attempts to measure the capacity of the liver in relation to nitrogen metabolism are not particularly satisfactory. The estimation of amino acids in the blood in cases of severe failure may show an increase in these values, but only

when obvious severe damage exists. Because the liver is intimately concerned with the formation of urea one can at times demonstrate a low blood urea figure in the presence of marked liver damage. Probably of greater significance is the increased ammonia content resulting from this inability to form urea. Here again such laboratory data are chiefly of value as confirmatory evidence of dysfunction, or as means of obtaining comparative data for following progress in a given case.

One important function of the liver lies in the control of normal blood coagulation. In prolonged obstructive jaundice, particularly, this function may be seriously altered with the associated danger of spontaneous or postoperative hemorrhage. Determination of the clotting time by any of the accepted methods provides a gross measure of some value. It is not a specific measure of liver function but at times gives valuable information. An accelerated sedimentation rate, although in no way a specific test of hepatic function, apparently is often of more value in indicating the possibility of hemorrhage and should be done where surgery is being considered in the face of obvious liver disease.

A final type of laboratory study is worth considering both as a measure of liver damage and as an indication for therapy. A type of secondary or hypochromic anemia is of common occurrence in serious liver disease of long standing and is not uncommon in the more acute forms of hepatic disorder. In the absence of definite bleeding, as from esophageal varices, such an anemia is an indication of the severity of the underlying process. In the more chronic forms it is difficult to treat and only large doses of iron are at all efficacious. Recently attention has been directed to the occurrence of a macrocytic type of anemia in liver disease. Such types are undoubtedly seen in the cirrhoses, particularly, and may represent a lack of storage of the hematopoietic principle found in liver. Liver therapy is certainly indicated in such instances but as a rule is not too successful.

I have obviously omitted mentioning many of the other tests of liver function but I have indicated what I consider the most important. As I have already intimated, the diagnostic value of such tests has been as a rule no greater than the clinical acumen of the man performing them. Repetition of any one or of several of them may provide valuable information regarding progress or prognosis in given cases.

Of greater importance in my estimation is the knowledge gained from the studies underlying the evolution of all of these laboratory procedures. From such studies, we are beginning to collect much of value as regards the principles of treatment. In liver insufficiency, whether acute or chronic, therapy must be directed toward correcting alterations in the numerous functions of this remarkable organ. First and foremost is the removal of specific liver poisons and putting the patient at absolute rest. Next in importance is, without question, the providing of adequate amounts of carbohydrate by mouth or by the intravenous route. Unless this supply of carbohydrate is really adequate, it is not possible to provide properly for liver cell repair and protection. In the sickest cases the administration of glucose by vein offers the surest means of supplying this need. Solutions ranging from 5 to 25 per cent glucose may be employed. Reasonable amounts of fluid are needed but, because of the danger of edema formation, excessive amounts are to be avoided. Relatively small amounts of fat in the diet are to be preferred because in the presence of jaundice the fat is not properly absorbed, with resulting gastrointestinal disturbances. Food rich in cholesterol should also be avoided. In spite of the frequent lowering of the serum protein large amounts of protein are to be avoided. The liver if damaged cannot properly deaminize the amino acids formed from protein digestion, and cannot properly form urea from nitrogenous material. Not until liver function has been sufficiently restored, if this is possible, will there be a restoration of normal serum protein values. The provision of generous amounts of glucose is the surest means of bringing about such a restoration of liver function. The protein in the diet should probably be limited to between sixty and seventy grams in the average case, whereas in patients suffering from serious, acute liver injury the carbohydrate intake may properly approach a level of 400 to 450 grams daily. Calcium therapy was hailed with enthusiasm as a means of treating the tendency to hemorrhage in patients with severe jaundice. Its use has proved extremely disappointing, although it may be of some value if combined with viosterol, as suggested by Ivy. When there exists an abnormality in the clotting mechanism due to hepatic failure, blood transfusion provides the most valuable form of treatment, in combination with adequate glucose therapy. In the more acute forms of liver insufficiency, glucose therapy also is the most important therapeutic measure for producing a diuresis if abnormal accumulations of fluid exist in the tissues or serous cavities. The use of diuretics, of which the mercurial preparations are the most effective, is indicated chiefly in those chronic liver disturbances such as portal cirrhosis, where the control of ascites and edema is a problem of prime importance.

The control of the anemia associated with diseases of the liver may involve the use of iron or liver, as already noted. Doses of sufficient magnitude are necessary for favorable results,

particularly in the more chronic forms of liver disease. In the more acute forms of serious hepatic failure there is little doubt that repeated transfusions are of very great value and are indicated for at least three reasons: first, to combat existing anemia and to improve general tissue function, secondly, to provide a certain amount of normal serum protein, and thirdly, to control spontaneous bleeding. Recently the group at the Mayo Clinic has reported favorable results from oxygen therapy in patients suffering from profound liver failure, with improvement in an associated anoxemia or oxygen unsaturation. One other measure, abdominal paracentesis, is obviously indicated where the presence of ascitic fluid is causing symptoms of importance.

Any or all of the above measures may be employed in given cases. In patients suffering from real liver insufficiency from any cause the use of such means of therapy, if instituted with promptness and carried out thoroughly, will produce striking results. Cases previously considered hopeless may be treated successfully. In support of such a statement I should like to refer briefly to the results obtained in a series of fifty-six cases treated at the Massachusetts General Hospital in the past fourteen years. These cases were selected in the sense that all of them were cases of extreme liver insufficiency and all were deeply jaundiced. In many instances a diagnosis of acute yellow atrophy was made and substantiated by autopsy. So far as we can judge by clinical and laboratory methods, the individual cases did not vary in severity during the different years from 1922 to 1936. The group of cases includes patients with alcoholic cirrhosis, toxic cirrhosis, arsenical jaundice, cinchophen jaundice, severe sepsis, and a few without any known cause. There were a few patients with intense obstructive jaundice due to stone. In every instance the patient was thought to be most critically ill. The severity of the disease in these cases is suggested by the fact that ascites and peripheral edema were demonstrated in twenty-five patients. Purpura was present in seven. Bilateral hydrothorax, a rare physical finding, was noted in two. Laboratory data showed that one-half of the patients had a serum bilirubin value of over 20 mg. per 100 cc., and three-quarters of those tested had a dye retention of greater than 50 per cent at the end of one-half hour. Out of thirty-nine patients surviving long enough to permit stool examinations, seventeen showed positive tests for occult blood with gum guaiac.

By all clinical and laboratory standards the patients included in this group were most seriously ill from hepatic failure, due to one cause or another, and survival in each instance was problematical. It is of interest, therefore, to examine the methods of treatment employed and the therapeutic results obtained. The group has been discussed in detail elsewhere and I will content myself with presenting the salient points.

From 1922 to 1925 inclusive, there were ten cases with nine deaths; from 1926 to 1929 inclusive, there were fourteen cases with fourteen deaths, or a mortality of 95 per cent during these eight years. During the years 1930 to 1935 inclusive, thirty-two additional cases were treated; of these twenty died, a mortality of 63 per cent. Inasmuch as many of the most severe cases were seen in the last period, it is important to determine the cause of such a striking drop in mortality. A study of the records shows that between 1922 and 1925 treatment consisted essentially in rest and the administration of a low fat diet. Glucose was administered by vein, subcutaneously or by rectum in small amounts on five occasions. Between 1926 and 1929 a diet designated as a high carbohydrate diet was ordered, and this diet contained a definitely higher carbohydrate content than the "low fat" diet. Glucose was administered rectally, subcutaneously, or by vein, in nine cases, but again in a very casual manner. From 1930 on, all the patients were on a very high carbohydrate diet, which was planned to contain as near to 400 or 450 grams of carbohydrate as the patient could take. In many instances, patients were so ill that only a small proportion of the diet could be taken. In twenty-six of the thirty-two patients, prolonged and intensive intravenous glucose therapy was carried out, in some instances a continuous drip being employed for many days. The drop in mortality coincided exactly with this period of persistent and intensive glucose therapy. A study of the laboratory data indicated that the depth of the jaundice bore absolutely no relationship to the mortality, nor did those patients with a high dye retention fare worse than those showing apparently better liver function as measured by this method. Ascites and edema, while obviously serious findings, did not determine the outcome. Of fourteen patients with ascites and no intravenous glucose, thirteen died; only seven out of eleven patients with ascites died after receiving adequate intravenous glucose treatment. The mortality of those patients who received intravenous glucose in large amounts for three days or more was under 45 per cent. Regardless of the severity of the individual cases, survival took place with sufficient frequency in the presence of enthusiastic intravenous glucose therapy to leave but little room for doubt that such treatment was the determining factor in lowering mortality. In this group of cases, purpura alone seemed to be an absolutely bad prognostic sign. Other methods of treatment, in addi-

tion to the use of large quantities of carbohydrate, were important in individual cases. In a few, repeated transfusions seemed to be of real benefit and in extreme hepatic failure such a procedure must be included as an important form of treatment. Anemia, purpura, spontaneous bleeding, and a low serum protein are the indications for its use. Diuretics were of little or no value during the period of acute liver insufficiency. Abdominal paracentesis was of symptomatic benefit only. In view of the previous remarks on the prognostic value of a spontaneous diuresis, it is of interest to note that in nine instances out of forty-one such an event occurred. All but one of these nine patients recovered. Of the twelve patients who survived between 1930 and 1935, eight showed a striking diuresis.

In summary, I should like to emphasize certain points. Aside from a few exceptional cases, the diagnosis of liver disease can be made and reasonably well evaluated by careful clinical observation alone. Repeated laboratory procedures afford information of real value in determining the progress of a given case. As a rule single tests do not give outstanding diagnostic or prognostic information, although they do give important confirmatory evidence of hepatic disease. The simple measurement of fluid intake and urine output in cases of real hepatic failure frequently provides the necessary evidence for arriving at a prognosis.

Treatment in all cases of hepatic insufficiency, regardless of their severity or cause, should consist in intensive carbohydrate therapy with free use of the intravenous administration of glucose. An additional measure of importance consists in multiple transfusions. By prompt and energetic treatment many cases of hepatic failure, even when progressing to acute yellow atrophy, may be saved.

CHAIRMAN SMITH: The discussion of Dr. Jones' paper will be opened by Dr. S. J. Thannhauser, Boston.

DR. S. J. THANNHAUSER, Boston: The concepts of liver disorders developed in a convincing manner by Dr. Chester Jones urge the idea of the greater value of clinical experience and judgment over any laboratory data concerning liver function. There is no doubt that every genuine physician will consent to this statement not only for liver diseases but also for all diagnostic consideration in medicine. What is the reason for such a disappointment in evaluating laboratory tests?

I think the last generation of physicians brought up in a splendid spirit of experimental medicine has awaited unrealizable responses from the laboratory work.

There cannot be "the test" of undisturbed function in any organ. Especially, the liver, composed of many units, different in anatomic structure as well as in functional task, cannot be checked by one or two test-tube reactions.

However, I would be wrong to minimize the value of chemical tests in favor of a refined clinical empiricism, obtained by intuitive and careful bedside observations. The liver has five main functions—the katabolic and anabolic transformation in carbohydrate in protein and in fat metabolism; the metabolic changes and probably the synthesis in the sterol series, that is cholesterol, bile acids and different vitamines; and last but not least the excretory function in the bile.

In checking these different functions we add to our bedside observations not only confirming figures but obtaining very valuable hints concerning the special kind of liver disorder. We have used, since our first publication ten years ago, with greatest satisfaction the quantitative determination of cholesterol and cholesterol ester to counterbalance the question of obstruction and liver drainage in urgent surgical cases as well as in patients with chronic jaundice. Total cholesterol alone is not of great value. Only the consideration of total in the relation to free and cholesterol esters gives the right points of diagnostic importance.

DIAGNOSTIC SCHEME OF CHOLESTEROL—CHOLESTEROL ESTER VALUE IN LIVER DISORDERS*

Total	Free	Esters	Ratio F:E	
High	High	High	Normal	Jaundice without liver damage, obstruction.
High	High	Lowered	Changed	Jaundice with liver damage, obstruction. Biliary cirrhosis.
Normal	Normal	Lowered	Changed	Liver damage without obstruction. Laennec annular cirrhosis.
Low	Lowered	Very Low	Inverted Ratio Ester Crash	Acute yellow atrophy. Severe toxic liver damage. Last stage of Laennec's cirrhosis.

Besides the cholesterol and cholesterol ester we check the direct and indirect coupling bilirubin according to van den Bergh and we determine the blood ammonia. The first test shows whether the bilirubin present in jaundice results from an obstruction of a bile duct or from lesions of bile capillaries (not in direct bilirubin) or if the bilirubin results from an alternation of the excretory function of the liver cells (that is indirect bilirubin).

The so-called icteric index expresses only in figures what is to be seen qualitatively with our eyes. Icteric index is only a statement of the degree of jaundice, not of the kind of jaundice, and should not be supposed to be an equivalent for van den Bergh's test.

An increase of blood ammonia concentration, which is present normally in the serum in a concentration of 0.02-0.04 mg. per cent as ammonium bicarbonate, is due to a lack of urea synthesis. The function of urea synthesis in the liver is a vital necessity to detoxify the poisonous ammonia ion that results from the deaminization of amino acids. An increase of ammonia ions in the serum is very harmful for the patient.

Considering the fact that the hepatic coma is prob-

*This table is a part of Dr. Thannhauser's discussion.

ably due to an ammonia poisoning resulting from a lack of urea synthesis, we must restrict the protein intake in patients with severe liver damage. High carbohydrate, as Dr. Jones already has emphasized, but very low protein is the advice to be followed in a liver diet.

CHAIRMAN SMITH: Is there further discussion from the floor? If there is no discussion we will pass on to the next paper.

Dr. Allen S. Johnson has been busy with chloride metabolism, and I think he has some interesting observations to tell us. Dr. Johnson.

SODIUM CHLORIDE THERAPY*

BY ALLEN S. JOHNSON, M.D.†

THE importance of sodium chloride, which makes up 0.17 per cent of the body weight expressed as Cl,[1] has been somewhat overlooked in our present-day interest in the more complex molecules of the hormones and vitamins. The ancients recognized both its dietary and commercial importance and salt even entered into religious ceremony.[2] There is considerable evidence that the migrations of some primitive peoples, like those of various animals,[1] have been determined by the quest for salt deposits as well as for food and water. The medical student is well aware of the rôle of these electrolytes in the various physicochemical systems of the body; the practicing physician is likely to overlook the importance of sodium chloride balance in various disease processes. Sodium chloride therapy is concerned primarily with making good a sodium or chloride deficit in the body which has occurred because of an inadequate intake or an excessive loss of these ions. It should be constantly borne in mind, however, that sodium chloride does not exist as such in the body fluids but as sodium and chloride ions whose individual concentrations may vary independently of each other in various conditions. Loss of either of these electrolytes, to which tissue cells appear to be impermeable, results in disturbance of osmotic equilibrium existing between the interior and exterior of the cells. In an attempt to restore this balance extracellular fluid moves into the cell or is lost from the body. The result, then, of loss of these ions, especially Na, from the extracellular fluids, is a decrease in the total effective intracellular fluids themselves with the resulting clinical phenomenon of dehydration. In most of the disease states in which NaCl therapy is beneficial, the object is to combat dehydration by restoring the lost extracellular fluid as well as the deficient electrolyte.

Food supplies the normal intake of sodium and chloride which amounts to 10-15 grams a day.[1] With a constant salt intake over an appreciable period of time the normal human being loses an equal amount so that his salt budget remains balanced even though there may be abrupt changes in his output from day to day. The kidney is the chief portal of excretion and appears to regulate the rate of output of sodium and chloride in order to maintain their normal concentrations in the extracellular fluids as well as in the blood plasma. There is a trifling loss of chlorides in the insensible perspiration but the sweat becomes an important vehicle of depletion only in the profuse sweating induced by hard physical work at high temperatures.[3] Except in severe diarrheas, like cholera and dysentery, no significant amount of salt is lost in the alvine discharges.[1] In these conditions, however, the resultant loss of sodium, chloride and water may progress to the point of profound shock described by O'Shaughnessy.[4] Finally, severe chloride depletion and dehydration may result from vomiting which removes large amounts of HCl from the stomach.

The collapse associated with acute intestinal obstruction was imperfectly understood until the experimental work of Haden and Orr[5] and of White and Bridge[6] showed that the dehydration resulted from the loss of fluids and especially chlorides by vomiting. The nature and origin of the hypothetical toxins responsible are still a matter of dispute but the importance of restoring lost chloride was well demonstrated by Hartwell et al.[7] and by Haden and Orr.[8] If parenteral saline is given in sufficient quantities to dogs with high intestinal obstruction, the usual period of survival is greatly lengthened even though the obstruction is not relieved. Today no competent surgeon would consider operating upon such a case without fortifying the patient with an abundance of sodium chloride by vein or by hypodermoclysis.

The same principles apply to vomiting due to other causes. It is important to remember, however, that the patient dehydrated by vomiting has lost acid rather than basic electrolytes. Ketone bodies may appear in the urine because exhaustion of glycogen reserves has caused an upset in normal fat metabolism; but, if the chloride loss is severe enough, a state of alkalosis, not acidosis, may really exist as Drake, Marsh and Gamble[9] have shown. The recognition of alkalosis in the presence of ketosis is important. The administration of glucose will relieve the ketosis but sodium chloride, not sodium bicarbonate, is needed to restore electrolyte balance. Sodium chloride adminis-

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tration has the further advantage of being applicable to either acidosis or alkalosis in such cases as the body is able to retain the ion needed and to excrete the other. The patient may thereby be spared the delay, and the physician the trouble, of actually determining whether acidosis or alkalosis has developed. If the persistence of vomiting prevents oral administration, equal parts of normal saline solution and 5 per cent glucose may be given parenterally. Advanced cases of deranged acid-base equilibrium, however, may lose their capacity for selective retention of the particular ion needed so that the oppositely charged but unneeded ion is also retained. In such cases the administration of a neutral salt like NaCl may fail to restore acid-base equilibrium. Here it may be necessary to determine by means of the CO_2 combining power of the plasma the exact nature of the acid-base derangement and to direct therapy toward restoring the particular ion which individual sodium and chloride estimations of the plasma show to be deficient.

Prolonged diarrhea may rob the body of both sodium and chloride as well as fluid, and restitution must be made by oral or parenteral routes if dehydration and shock are to be avoided. Similar precautions are indicated if an enterostomy is allowing an escape of chlorides from the upper gastrointestinal tract. The normal organism attempts to balance its sodium chloride budget by reducing the renal output of salt. Before the extracellular fluids and the blood stream become seriously depleted of sodium and chloride, however, the urinary sodium chloride output will have fallen to zero. In these cases, as in heat cramps,[10] enough salt should be given orally or parenterally to secure a renal output of three grams of sodium chloride a day as this seems to represent an adequate margin of safety.

Talbott and Michelsen[10] have shown that heat cramps are due to "a loss of base, chlorides, and water from the body principally by way of the sweat glands without adequate replacement of the same". It is "essentially an occupational disease and an industrial hazard is created by the association of hard work, high external temperature, and profuse sweating". There is rapid amelioration of symptoms if the diminished concentration of chloride and base in the blood and body tissues is restored by the administration of sodium chloride. This may be given orally in doses of fifteen to twenty grams in the form of enteric coated tablets and in the severe cases 3000 cc. hypodermoclyses of normal saline may be administered. Even more satisfactory is adequate prophylaxis which consists of administering sodium chloride in food, tablets, and drinking water to workers exposed to high temperatures. An abundant sodium chloride intake is especially important during the first few days. Subsequently, after acclimatization, some compensatory mechanism comes into play whereby a more dilute sweat is secreted so that a salt intake of about fifteen grams a day will maintain sodium chloride equilibrium.[11] The mechanism underlying heat stroke is apparently quite different as prostration and death may occur before the acid base equilibrium is seriously disturbed and intravenous saline may actually make the convulsions worse.[12]

As long ago as 1874 Hilton Fagge[13] of Guy's Hospital, London, treated a case of diabetic coma by the intravenous injection of saline solution. This procedure was based on his recognition that the state of dehydration and collapse was essentially similar to that studied by O'Shaughnessy[4] in cholera. In diabetic acidosis, base and water are lost through the kidneys along with the excretion of ketone bodies and glucose. Loeb and others[14] have shown that denial of insulin to a diabetic has no effect on water and electrolyte balance so long as no appreciable glycosuria develops. When followed by marked glycosuria, with or without ketosis, there is loss of water, sodium, potassium, and chlorine associated with loss of weight and nitrogen. Restoration of lost base and fluids by means of normal saline hypodermoclysis has now largely replaced the administration of alkalies in diabetic acidosis.[15, 16] Insulin and proper dietary regulation are of paramount importance in adjusting carbohydrate metabolism but the restoration of normal electrolyte balance depends on the administration of sodium chloride and water. There are a few clinicians, however, who prefer to supplement the insulin, carbohydrate therapy of diabetic acidosis with isotonic solutions of sodium lactate and Ringer's solution rather than with sodium chloride alone on the ground that the acidosis is thereby more quickly relieved.[32]

"The syndrome of salt loss, dehydration, and the resultant state of shock, typical of these disturbances, is characterized clinically by progressive weakness and overwhelming prostration, nausea and vomiting, increasing pulse rate with falling blood pressure, subnormal temperature, sunken eyes, and loss of the normal turgor of the subcutaneous tissues."[17] The recognition of the similarity of this syndrome to that of Addison's disease has guided the experiments which have demonstrated that insufficiency of the adrenal cortex results in an abnormal renal excretion of sodium and chloride. This leads eventually to such depletion of the body's supply of these electrolytes as to produce dehydration and its inevitable chain of consequences. Apparently the adrenal cortex serves as a regulator of sodium metabolism. Loeb further says,[17] "The most convincing evidence for the value of salt as a therapeutic measure in adrenal dis-

ease in man, as well as in the adrenalectomized animal, is found in the fact that the withdrawal of salt may induce acute adrenal insufficiency and that frequently the only therapeutic measure necessary to relieve it is the re-administration of sodium chloride. Nevertheless it should be recalled that salt alone will not maintain the normal sodium level in the blood or cause indefinite survival of the completely adrenalectomized animal. In other words, a certain amount of cortical substance, either formed within the body or introduced from without, is essential to life."

The value of sodium chloride therapy in pneumonia has been disputed ever since 1899 when Penrose[18] first reported beneficial results from its use. In 1913 Peabody[19] showed that prior to the crisis in lobar pneumonia the blood chlorides and urinary chlorides undergo a marked decrease. Haden[20] in 1927 reported benefit from sodium chloride administration in a small series of lobar pneumonias. Many observers who have interpreted these biochemical findings as an indication of chloride retention by the tissues sound a note of warning against such therapy for fear of producing serous effusions and edema, especially of the already congested lungs.[21] Sunderman's observations[22] have helped to reconcile these divergent opinions. Pneumonia is characterized not by a retention of chloride during the precritical period but by the body's diminished capacity to conserve chloride on a low intake of chloride and a diminished capacity to excrete excess chloride on a high chloride intake. The low blood and urinary chlorides before the crisis are apparently due to a deficient chloride intake associated with the anorexia of the patient. After the crisis the balance becomes restored as a result of an increased salt intake and the return of the kidney's capacity to adjust sodium chloride excretion to the needs of the body. The practical therapeutic conclusions to be drawn from these observations are uncertain. Wilder and Drake[21] advise giving children an amount of sodium chloride which will cause enough water retention to prevent weight loss. This is difficult to determine in the case of adults as few beds are mounted on scales. A middle course is probably the wise one at present. Salty broths may be given at frequent intervals in addition to the monotonous round of tap water and fruit juice which constitutes the usual saltless diet of the pneumonia patient. Intravenous drips of normal saline should probably be reserved for cases of impending dehydration or peripheral circulatory collapse where it is imperative to augment the volume of circulating fluid.[23]

The behavior of the blood chlorides in cutaneous burns has features in common with the phenomena observed in lobar pneumonia. The period prior to the separation of the devitalized tissue resembles the precritical stage of pneumonia in that there is a lowered blood chloride level and a lessened urinary chloride output. The NPN is elevated in spite of an increased nitrogen output in the urine. The lowering of the blood chloride is proportional to the amount of tissue devitalized and cannot be attributed to loss of serum from denuded surfaces as it occurs even in the presence of a perfectly dry eschar. After separation of the devitalized tissue, even though there is a marked increase in serous oozing, the blood chloride rises to normal and there is a sudden outpouring of chlorides in the urine similar to the postcritical stage of pneumonia. Davidson[24] believes that retention of sodium chloride takes place in the body and concludes that the fall in the blood sodium chloride cannot be wholly explained by alteration of renal threshold, diet, fever, exudation, blood concentration, or vomiting. He recommends sodium chloride therapy, though its rationale is obscure, if retention already exists. All observers agree with Underhill and others,[25] however, that dehydration and blood concentration must be prevented. The tannic acid or gentian violet treatment of the burned area will produce a coagulum to prevent fluid loss. A high fluid intake is an important adjunct. If this is to be given parenterally, normal saline is of course indicated. If oral administration of fluid is to be relied upon, sufficient sodium chloride should be given with the diet to maintain a constant body weight, thereby insuring normal fluid retention by the tissue.

In 1922 Schlagintweit and Sielmann[26] observed a dilution of the blood and a lowering of the blood chloride level in patients suffering from x-ray intoxication following deep radiation therapy. Cameron and McMillan[27] did not find the blood chlorides invariably affected though they did observe a diminished chloride and increased nitrogen excretion in the urine. Both groups of investigators agreed that an increased sodium chloride intake would prevent or relieve the symptoms. At the present time radiologists appear to depend more on a liberal sugar intake for several days prior to radiation.

It has been known for a quarter of a century that chloride administration hastens the elimination of bromine and iodine from the body whereas chloride-poor foods slow this excretion.[28] Wile, Wright and Smith[29] were among the first to apply this biologic fact to the therapeutics of bromide intoxication. Since that time various investigators[30] have employed sodium chloride in the treatment of bromide intoxications and dermatoses. A nutritious, easily assimilated diet, rich in vitamins, is prescribed along with a high fluid intake. Ten grams of sodium chloride is given daily in addition to

the salt contained in the ordinary diet. Except in emergency parenteral saline is contraindicated as Wile[31] believes that the rapid elimination of bromine may cause damage to the kidneys.

During the past year I have been interested in a group of seventeen patients with a fatigue syndrome having certain points in common with the symptom complex often referred to as chronic exhaustion, nervous exhaustion, neurasthenia, or neurocirculatory asthenia. The chief complaint, common to all seventeen patients, has been weakness and easy fatigability with a disinclination for physical activity, especially if it involve sustained exertion. Most of them complained that they failed to feel refreshed even after a sound night's sleep; and the males who have previously had athletic inclinations find that they can no longer "get into condition" by means of progressive graduated exercise. More than half of the patients have complained of increased nervousness and irritability although this symptom is more often appreciated in retrospect when the patient becomes aware of greater calm and poise after the institution of therapy. The onset is insidious and the duration difficult to define. The severity of the symptoms may vary from unusually slow recuperation from the fatigue of exercise to almost total incapacity for physical exertion. Precordial pain, palpitation, and sometimes definite exertion dyspnea may be experienced. Three quarters of the patients were in the twenties and thirties and there was a slight preponderance of females. None of them had any clinical evidence of coronary disease or other organic pathology and such metabolic readings as were obtained were normal. The pigmentation, hypotension, hemoconcentration, and gastrointestinal disturbances of Addison's disease were absent. The one laboratory finding common to all these cases has been a low blood chloride level although there is no evident cause for this, such as excessive chloride loss by any of the usual channels of excretion or an obviously deficient chloride intake. The significance of the low blood chlorides, which are below 450 mg. NaCl per 100 cc. of whole blood, is obscure. An increase of two to six grams in the patient's daily sodium chloride intake is followed in four or five days by complete relief of the presenting symptoms. Conversely, deprivation of this extra salt is followed after a like period of time by a reappearance of the symptoms. These observations have been carried out repeatedly on various patients in this group with identical results even when they were not warned what to expect. But in neither the salt administration phase nor in the deprivation phase is there a significant change in the blood chloride level. Observations on the chloride output of these cases have not been entirely satisfactory as they were all ambulatory private patients, but in general it may be said that sodium chloride therapy is attended by an increased urinary chloride output commensurate with the increased chloride intake. Usually a patient gains about two pounds of weight during the first fortnight of therapy but there is no further gain. The blood pressure remains unchanged. Unfortunately the sole criterion of successful therapy seems to be the subjective improvement reported by the patient. Nevertheless the seventeen patients in question have been relieved of their fatigue symptoms for periods varying from four months to one year by the simple expedient of increasing their salt intake. No relapse has been experienced except when salt deprivation was deliberately carried out. Low blood chlorides, however, cannot be regarded as the sole diagnostic criterion of this syndrome, as they have been found in various constitutional disorders whose presenting symptom was fatigue. Among these may be mentioned cases with chronic infection, secondary anemia, coronary disease, and schizophrenia. Such cases have not been benefited by salt therapy alone. It would appear that sodium chloride therapy is purely empirical in the fatigue syndrome described and it is indicated only in those cases of fatigue with hypochloremia and signs of neurocirculatory instability in which careful study fails to reveal any recognized constitutional disorder to account for the presenting symptoms.

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CHAIRMAN SMITH: The discussion of this paper will be opened by Dr. Allan M. Butler of Boston.

DR. ALLAN M. BUTLER, Boston: Dr. Johnson has called your attention to many of the conditions in which disturbances in the sodium and chloride balances and plasma concentrations indicate sodium chloride therapy. In discussing this subject I wish to emphasize one point. If one is to appraise adequately, and treat, disturbances in the metabolism of sodium and chloride, these two substances must be considered as two dissociated, oppositely charged ions, Na+ and Cl—, and not as a single substance, sodium chloride. Before sodium could be determined conveniently it frequently was the custom to report chloride values as so many grams of sodium chloride. Such data give no information concerning sodium or sodium chloride. Indeed one cannot determine the concentration of undissociated sodium chloride in plasma or body fluids because this does not occur. We determine concentrations of serum calcium and serum phosphorus, not of serum tricalcium phosphate. The plasma *sodium* concentration is roughly 1.3 times that of the plasma *chloride*. On the other hand, the red blood cell *chloride* concentration is less than the *plasma chloride* concentration but roughly thirteen times its sodium concentration. In other tissues, so far as our knowledge goes, the absolute and relative concentrations of sodium and chloride are still different. Making deductions from the information derived from plasma, the concentration of sodium *or* chloride in the body fluids may vary independently. To be sure, if their relative plasma concentrations are altered, a situation usually arises which results in the kidney excreting the one and conserving the other in such manner as to tend to re-establish their normal plasma concentration ratio. As a result of such a regulatory mechanism urine may be practically free of the one ion, while containing considerable amounts of the other. The stool concentrations of sodium and chloride are likewise unequal.

To illustrate the desirability of considering the separate distribution and metabolism of these two ions within the body, we will take two examples.

First, Dr. Johnson has called your attention to his series of patients in whom he has observed a low blood chloride. The whole blood chloride concentration per unit volume of blood depends upon three factors: first, the concentration of chloride in the plasma; secondly, the concentration of chloride in the red blood cell; and thirdly, since concentrations in plasma and red cells are different, blood chloride concentration depends upon the volumes per cent of red blood cells. Hence whole blood chloride concentration varies with variation in the hematocrit even though plasma and red blood cell chloride concentrations remain normal. Therefore, Dr. Johnson's observation raises certain questions. First, what is the plasma chloride concentration in these patients? Though an answer would give us a quantitative variation from the normal, alone it would not tell us much. Is there an associated acidosis or alkalosis? Is there an associated alteration in plasma sodium which affects the plasma bicarbonate as much as does the altered plasma chloride? Since the determinations of plasma sodium, pH and bicarbonate are today as simple as the determination of plasma chloride, these questions, pertinent to an understanding of an observed low blood chloride, can be readily answered. Possibly one would like to know the concentration of chloride in the red blood cells, but present knowledge indicates that no helpful information would be derived therefrom.

The second example concerns the efficiency of the treatment of alkalosis and acidosis by the administration of parenteral physiologic saline. Dr. Johnson has called your attention to the loss of chloride in excess of sodium in the vomiting of gastric secretions and the resultant alkalosis. As well as the chloride lost by the vomiting, the patient will have lost sodium in the urine, for, in the early phases of the vomiting before severe dehydration has set in, sodium will be excreted in the urine in an attempt to resist the alkalosis. Later when dehydration is severe, sodium will not be excreted in the urine even though the continued loss of gastric chloride produces a severe alkalosis. This is the situation when one resorts to parenteral physiologic saline therapy. In the saline solution the ratio of sodium to chloride is 1 to 1 whereas in plasma it is 1.3 to 1. Since physiologic saline has a sodium or chloride concentration equal to the plasma sodium (not chloride), the chloride concentration of physiologic saline is hypertonic to the plasma chloride. Thus at the beginning of hydration therapy when the kidneys are not functioning, physiologic saline is ideal since it provides chloride in excess of that required to balance the sodium and thus corrects the excessive chloride deficit and alkalosis. When the saline therapy has replaced the sodium deficit, the body will be sufficiently hydrated to provide a blood and urine flow permitting adequate kidney function. If a chloride deficit still exists, the kidney will then excrete a large amount of sodium in an alkaline urine without excreting chloride. Thus from start to finish in cases of this type, the administration of physiologic saline, plus glucose for the starvation ketosis, is as near perfect therapy as possible.

On the other hand, if we have a patient who has a severe acidosis with loss of base, principally sodium so far as the blood plasma and extracellular

fluids are concerned, the parenteral administration of sodium chloride will provide an excess of chloride over sodium in terms of the requirements of increasing plasma and extracellular volumes where 1.3 times more sodium is required than chloride, even when no acidosis is present. Physiologic saline alone or diluted with glucose may, therefore, accentuate the acidosis by an elevation of plasma chloride or drop in plasma sodium unless this relative excess chloride is promptly removed by the kidney. As any acidosis severe enough to require parenteral therapy is attended with such dehydration as to impair kidney function, it is clear that the treatment of acidosis by parenteral physiologic saline may in the initial stages of such treatment accentuate the acidosis. Therefore, in acidosis the administration of a solution of sodium bicarbonate or an oxidizable organic sodium salt is indicated at the beginning of hydration therapy if the best results are to be obtained. Where such a solution must be given parenterally, as is usually the case if parenteral saline is being administered, the use of sodium lactate is at the moment the most convenient and effective therapy. A solution of this salt is available in sterile ampoules which upon being diluted as prescribed can be injected intravenously, subcutaneously or intraperitoneally with the physiologic saline without causing irritation. By its use in conjunction with saline and glucose, the acidosis and hyperpnea may be overcome in the initial stages of the treatment. The possibility of a chloride acidosis will be avoided, and previous to the establishment of a kidney function capable of selectively excreting chloride and conserving base, the kidney's attempt to excrete the excess chloride of the parenteral saline will not cause a wasteful loss of sodium in the urine.

Usually the differential diagnosis of alkalosis and acidosis can be made from the history including the character of the fluids administered to the patient and from the type of respirations. Occasionally an overwhelming toxemia may inhibit the compensatory hyperpnea of acidosis. When in doubt as to the presence of acidosis or alkalosis in a severely dehydrated patient, the use of a solution containing sodium chloride plus sodium lactate in such amount as to make the absolute and relative concentrations of sodium and chloride those of plasma is far better therapy than the parenteral administration of physiologic saline. Since, as well as the sterile ampoules of sodium lactate, there are on the market sterile ampoules of saline plus sodium lactate in proper proportions, there is now available to all physicians a convenient and more effective parenteral fluid therapy for acidosis and dehydration than results from saline alone.

CHAIRMAN SMITH: Dr. Bock, would you like to say anything on this subject? If not, I will ask if there is any further discussion?

DR. J. M. LOONEY, Worcester: *Mr. Chairman*—These very excellent papers which have been given to us on sodium chloride therapy lead one to believe that this subject is just beginning to come into the prominence which it deserves. The whole phase of sodium ions and chloride ions is not to be understood, however, without taking into account certain other ions of the body. A recent paper on the metabolism of sodium and potassium given at New York has indicated that probably this entire field of therapy is to be explained, not from the loss of sodium chloride, but from the changed ratio between potassium and sodium. Recent work has shown that totally adrenalectomized animals can be maintained indefinitely by giving sodium chloride and sodium citrate and that, if these animals are given as little as half a gram of potassium, they can be thrown into very severe adrenal shock and death will result. The loss of sodium chloride in cases of heat exhaustion resembles that in cases of adrenal insufficiency and the cure by giving sodium chloride is undoubtedly due to the fact that the potassium of the body is maintained in the tissues of the cells, whereas the sodium is predominant in the fluids. In these cases where fluid sodium is lost, there results an overbalance of potassium and by giving sodium the potassium overbalance, which undoubtedly seems to be the cause of the symptoms, is overcome. One of the major functions of the adrenal gland appears to be that of regulating the balance between sodium and potassium which is necessary for the normal functioning of many physiologic functions.

CHAIRMAN SMITH: Is there further discussion from the floor?

Most of us want to be specialists or experts or something of that sort, but there are still a few men in medicine who are satisfied with a reputation of an outstanding general practitioner. Such a man is Dr. Sproull of Haverhill, who will tell us the general practitioner's view on the treatment of angina pectoris. Dr. Sproull.

A GENERAL PRACTITIONER'S VIEWS ON THE TREATMENT OF ANGINA PECTORIS*

BY JOHN SPROULL, M.D.†

I HAVE chosen the title of this paper, namely, "A General Practitioner's Views on the Treatment of Angina Pectoris" because I am a general practitioner and I am presuming that the larger part of this audience is composed of similar general practitioners. I propose to present to you today the approach to this problem and the details of treatment of this syndrome, angina pectoris, which I use in my daily work as a general practitioner of medicine in a suburban city of moderate sized population.

Some of the assertions I shall make, you will immediately subscribe to because they will be in accord with your experiences, others you will accept because they appeal to your reason, and others still you will accept only tentatively, believing, I hope, in my veracity but not completely accepting these statements until such times as you have tested their accuracy in the crucible of experience, the daily practice of medicine.

At the outset certain postulates may be stated:

1. Angina pectoris is not a disease entity but a painful, subjective syndrome associated with various pathologic alterations and functional

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†Sproull, John—For record and address of author see "This Week's Issue," page 469.

disturbances of cardiac musculature and its nutritional circulation.

2. The syndrome is of very common occurrence and its presence rather than the associated pathologic condition causes the patient to seek the aid of the practitioner of medicine.

3. Because of its common occurrence the large majority of cases of angina pectoris come under the care of the general practitioner.

4. As a corollary of the preceding postulates it follows that every general practitioner should have a clear conception of the methods of production of the syndrome and a comprehensive knowledge of the various pathologic conditions with which the syndrome is associated.

5. An understanding of the associated pathologic and disturbed functional conditions should establish the basis for the formulation of the rational treatment of this common complaint.

6. It would seem self-evident that, for a syndrome of such common occurrence, a preconcerted method of treatment based on an understanding of the altered anatomic and physiologic conditions should be possessed by every general practitioner.

In practice a classification of the anginas according to the associated pathologic conditions has proved an excellent method of approach and the following classification which covers the various groups met with is suggested.

Group 1. Those anginas associated with atherosclerosis of the coronary arteries or their branches. This group may be termed the ordinary, everyday "garden" variety and embraces by far the largest number and is far and away, because of its great frequency, the most important.

Group 2. Those associated with syphilis of the aorta.

Group 3. The cases associated with disturbances of rhythm characterized by marked increase in the rate of the heart beat.

Group 4. The anginas occurring with diseases of the blood, commonly severe anemia, but also the rarer disease polycythemia vera.

Group 5. Comprises the cases associated with the therapeutic administration of insulin in patients with diabetes mellitus.

This classification embraces practically all the cases which a general practitioner will be called upon to treat. For clearness each group will be discussed separately and in reverse order to the positions assigned in the grouping.

Group 5. The cases of angina pectoris associated with the therapeutic administration of insulin in cases of diabetes mellitus. In these cases the production of the syndrome is probably dependent upon hypoglycemia caused by overdosage of the therapeutic agent. The incidence of this group of anginas is not large for the reason that the total number of cases of diabetes mellitus seen by a physician in general practice is small and but few of those who receive insulin develop angina pectoris. The recognition of this group depends on estimations of the blood sugar and the treatment is clearly the regulation of the dosage of insulin to maintain a normal level for this blood element. It is of importance, however, to realize that angina pectoris not dependent on hypoglycemia is of common occurrence in diabetic patients, more so probably than in the ordinary run of people of a similar age.

It is asserted that atherosclerosis occurs with unusual frequency in individuals with this metabolic disease and that atherosclerosis of the coronary arteries is of equally common occurrence, and if this is so, it is clearly evident that angina pectoris is likely to be a common complication of diabetes mellitus and that its occurrence in patients with diabetes taking insulin is usually due to the associated coronary artery disease and not related to the administration of the therapeutic agent. The occurrence of coronary artery disease being a causative factor in the production of anginas in this group explains why the cure or arrest of the diabetic process has no specially favorable influence on the angina other than that obtained by the reduction of obesity, a condition often found in diabetes.

Group 4. The group associated with diseases of the blood includes the cases (not uncommon) occurring with severe anemia but also the rarer cases accompanying polycythemia vera. The treatment for these anginas is evidently the treatment of the blood dyscrasia. Polycythemia vera is not usually listed as a cause of angina pectoris but two cases of quite severe angina due to this cause have been observed personally, the latter one of the two dying of typical coronary thrombosis.

Group 3. Those cases associated with and apparently causatively related to the presence of disturbances of the rhythm of the heart and chiefly the disturbances of rhythm characterized by marked increase in the rate of the heart beat are probably larger in number than is at present recognized. Many practitioners are not aware of the existence of this group and yet its recognition is a matter of great importance, for the treatment is the treatment of the disturbance of rhythm (the causative factor) and differs fundamentally from the usual treatment of angina pectoris.

Paroxysmal tachycardia has been the only disturbance of rhythm personally encountered as such a causative agent, although other disturbances of rhythm playing a similar rôle have been reported.

The treatment of anginas in this group is

usually so successful that it is deemed necessary to urge the importance of its recognition.

The diagnostic clue observed in each case has been the patient's awareness for a period of time of varying duration of rapid beating of the heart before the onset of the angina, and it is therefore advised as good practice to make direct questioning of all angina patients as to the occurrence of such rapid beating, for some patients will not offer such information believing it is of little importance compared with the description of their agonizing pain.

The anginal pain in this group may be of such severity and duration as to simulate coronary thrombosis and require large doses of morphia for its relief. Furthermore, there may be associated coronary artery disease proved by electrocardiogram and yet the paroxysmal tachycardia and not (as usual) the coronary artery disease may be the initiating factor in the production of the attack of angina.

In such cases, treatment directed toward the coronary artery disease may be of no avail; but if the presence of paroxysmal tachycardia as the causative agent be recognized, treatment directed to this condition may bring about complete cessation of the anginal attacks.

Group 2. The anginas associated with syphilis of the aorta constitute one of the two major groups, the other being group No. 1, namely, those associated with atherosclerosis of the coronary arteries or their branches.

It is difficult to estimate what percentage of anginas are related to aortic disease. There is considerable difference of opinion as to the incidence of syphilitic aortitis.

Some believe that aortitis is a comparatively rare disease and others that it is quite common. The reliability of general mortality statistics as to the frequency of occurrence of this disease may be justly questioned, and for the following reasons:

1. Syphilitic aortitis as a disease entity has no practical existence for most general practitioners unless accompanied by valvular disease or aneurysm, and yet the disease occurs about twice as frequently without valvular involvement as with it, and also much more frequently without aneurysmal formation.

2. It is difficult, and many general practitioners are unable, to recognize any other than the most apparent regurgitant murmurs which accompany aortic valvular disease due to syphilis, and thus a great many cases with faint murmurs escape detection.

3. It is not the custom or habit of practitioners in general to make or have made serologic tests for syphilis even in cases of angina pectoris.

4. Autopsies to determine the cause of death are of infrequent occurrence outside of large hospitals and many cases of syphilitic aortitis die with the disease wholly unrecognized.

5. Granting the recognition of syphilis of the aorta as the cause of death, the stating of such a cause on death certificates makes for so many social difficulties, like loss of insurance and disturbance of family relationship, that some substitute other causes such as myocarditis, arteriosclerosis, or valvular disease of the heart. However, be the aforesaid statements true or false, there is an admitted group of angina pectoris cases apparently causatively related to syphilis of the aorta. Several facts are worthy of note in this connection.

1. It is well known that syphilitic processes probably seldom if ever invade the coronary arteries per se.

2. It is equally well known that syphilis does show predilection for the first portion of the ascending aorta, the portion from which the coronary arteries arise.

3. Syphilitic involvement of this portion of the aorta does produce in some cases narrowing or closure of the opening or openings of one or both coronary arteries, thus interfering with the nutritional blood supply to the heart, and such narrowing may be the result of syphilitic inflammatory exudation, gummatous formation or scarring of previously present syphilitic ulcerations.

4. Atherosclerosis of a coronary artery or its branches may occur coincidentally with, but not dependent on, the syphilitic aortitis and such atherosclerosis of the coronary artery rather than the coexistent syphilitic aortitis may be the cause of the anginal symptoms. It seems probable that such a combination of pathologic processes obtaining, offers an explanation why antisyphilitic medication fails to give relief in some cases of angina pectoris when serologic and other tests prove the existence of syphilitic aortitis.

The treatment of angina pectoris dependent on syphilis of the aorta is the treatment of syphilitic aortitis. It is advised, however, that the treatment in this group of cases differs only from the largest of all groups, namely, those associated with atherosclerosis of the coronary arteries in the matter of drug treatment.

Because of the sovereign nature of the remedies we possess against syphilis, the use of all other accessory measures is often relegated to the background or neglected entirely, although the exhibition of these so-called accessory measures is just as much indicated in this group as in that group dependent on atherosclerosis of the coronary arteries. To state the matter fully, while commending the use of antisyphilitic medication, the modification of the patient's habits as to eating, drinking, muscular exertion, work, rest, and emotional dis-

turbances is of great importance. These measures will be dealt with fully farther on in this presentation.

The drug treatment of syphilitic aortitis is comparatively well standardized and should consist in the exhibition of potassium iodide in large doses in conjunction with the administration of mercury or bismuth for a period of eight weeks, during which time no arsenicals should be administered.

The dosage and method of administration of the foregoing advised drugs are deemed important. The dosage of 75-150 grains of potassium iodide given in three divided doses after meals is deemed adequate. The initial dose is better large. The custom of beginning with small doses and increasing gradually is unnecessary and at times harmful.

The exhibition of mercury may be either by intramuscular injection or by inunction. A preference for the latter method has been the outcome of unfavorable results with the intramuscular injections.

The adequacy of the inunction method of administering mercury is unquestioned, while the inadequacy of some preparations advised for intramuscular injections of the same drug has been proved. Certainly no preparation or method of administration of this drug can be considered adequate unless the physician can by overdose produce evidence of mercurial intoxication. Measured by such standards, mercurial inunctions are potent and adequate and some preparations for intramuscular injection are decidedly lacking in efficiency.

Bismuth given by intramuscular injection is reported by some authorities as being more valuable than mercury in this disease, and yet it may not be denied that mercury adequately administered remains as ever a powerful antisyphilitic medicament.

At the expiration of eight weeks' treatment with the aforementioned drugs, arsenicals may be usually administered with safety, provided the initial dose is small and that the dosage is very gradually increased to a level always some degree below that used in the treatment of syphilis in other parts of the human body.

Various arsenical preparations are available. The selection of any particular one is not part of this paper.

The rotation of a course of the preliminary drugs, potassium iodide and mercury, with a course of arsenicals may be continued for a year, after which treatment is probably better given intermittently with a considerable period of time between courses of treatment. Occasionally angina pectoris cases of this group will derive more benefit from the drugs advised in the atherosclerotic cases than from the so-called antisyphilitic drugs.

Group No. 1 in this classification embraces those cases of angina pectoris associated with atherosclerosis of the coronary arteries or their branches and includes by far the largest number of anginas with which the practitioner has to deal. It may be termed the ordinary everyday "garden" variety and probably represents about 85 per cent of all anginas met with in daily practice. Because of its frequency of occurrence a knowledge of the underlying pathologic conditions and the results ensuing therefrom is important.

Atherosclerosis of any artery produces a thickening of the vessel wall because of pathologic changes present principally in the subintimal tissues of the vessel affected, with a consequent narrowing of the lumen and loss of the normal elasticity of the vessel. In addition, the smooth endothelial lining of the blood vessel in part or in toto may be replaced by rough, irregular areas of atheromatous ulceration and subsequent calcification.

It will, therefore, be readily understood that such narrowing or obliteration of the lumen of a coronary artery, or of one or more of its main branches, whose function is to carry arterial blood to the heart muscle, must seriously interfere with the adequacy of the nutritional blood supply to the heart muscle and especially so when unusual muscular work or emotional stress makes unusual demands for increased blood supply to the heart, which increased blood supply cannot be furnished because of the inadequacy of the artery as the result of its diminished calibre due to the existing atherosclerosis.

In addition, the presence of roughening of the intima of the vessel as the result of atheroma or calcification, not only further impedes the flow of blood but also favors the formation of blood clot, thus facilitating the production of that serious disease, coronary thrombosis.

It may, therefore, be stated that the production of the syndrome angina pectoris in this group is dependent in the greater part on inadequate blood supply to the heart, dependent in turn on lessening of the lumen of the affected coronary artery or arteries. It may also be said that in the present state of medical knowledge there is no known method by which the arterial pathologic changes causing this inadequate blood supply can be altered. There is no known method of therapy which will cause any decrease in the atherosclerotic processes in the coronary arteries or their branches, or any enlargement of the lumen of such diseased arteries. A realization of the truth of this statement is important and necessary for the formulation of a plan of rational treatment for the syndrome angina pectoris.

It should be apparent that the proper treatment of a syndrome associated with dysfune-

tion of the vital organ, the heart, produced by an inadequate blood supply dependent on unalterable pathologic conditions in the structure of the affected arteries is the regulation of all that constitutes life for the individual who manifests the syndrome upon a level and at a rate in inverse ratio with the degree of inadequacy of the blood supply. That is to say, the greater the impairment of the blood supply the lower must be the level and the lesser the rate at which the affected individual should live. An appreciation of the foregoing statements and their implications should form the basis for the details of the rational treatment of this distressing syndrome. Furthermore, while believing firmly in the efficacy of drugs as part of the treatment of the condition under consideration, it would seem that the regulation of the patient's life upon the level and at the rate previously mentioned, can hardly be overemphasized.

The details of treatment of this group of anginas will be considered under several headings:

1. The treatment of the attack.
2. The treatment between attacks consisting of measures directed toward lessening the frequency or diminishing the severity of the attacks, or both, or, still more to be desired, the complete abolition of the attacks. The treatment of the attack is well standardized. In the early stages of disability, most attacks are dependent on unusual muscular exertion or unusual emotional stress.

A cessation of the causative muscular exertion by simple rest or removal of the cause of the emotional disturbance, will usually of itself give ready relief.

As the condition progresses, other measures are usually necessary. These other measures are so well known that it is only for the purpose of completeness they are mentioned.

1. Nitroglycerin in doses of 1-200 to 1-100 of a grain under the tongue usually gives prompt relief. It is better administered in the readily soluble tablets made for subcutaneous injection.

Many patients suffer considerable discomfort from the dosage of 1-100 of a grain and for these the dosage of 1-200 is probably better. Christian[1] suggests that as soon as the patient feels relief from his anginal pain, the undissolved portion of the tablet be removed, thus lessening the headache and tinnitus and flushings from which many patients suffer when taking nitroglycerin.

2. Alcohol is at times valuable in giving relief from the acute attack. A swallow of undiluted whiskey or brandy is the method of choice for its administration.

3. If none of these measures prevail, the subcutaneous administration of morphine sulphate in dosage sufficient to alleviate the evident suffering is indicated. Usually, but not always, one-fourth of a grain of morphine sulphate administered hypodermically will be adequate.

The latter method of giving relief should always be used reluctantly and with full appreciation of the truism that any case of angina pectoris of such severity or of such persistence as to require morphine for its relief is to be regarded as a probable case of coronary thrombosis until proved otherwise.

Comparatively few cases of angina pectoris require morphia for relief, while most cases of coronary thrombosis do. Many patients, however, by regulation of their lives by such measures and in such manner as will be indicated get such diminution in severity and lessening of the incidence of attacks that the aforementioned advised measures are seldom needed. Indeed it would seem right that this should be so, for while lacking experimental proof of the truth of the hypothesis it seems rational to believe that repeated insults to the cardiac musculature as endured in attacks of anginal pain must be harmful, even if such attacks are brought to speedy terminations by the administration of nitroglycerin or other drugs.

Treatment between the attacks has for its purpose either the abolition of them or the alleviation of them either as to frequency of occurrence or as to severity or as to both and should be considered under several headings.

1. The attitude of the physician to and with the patient.
2. The regulation of the patient's life considered under sub-headings:
   a. Work, exercise and rest.
   b. Obesity, diet and dietary habits.
   c. Emotional regulation.
   d. Miscellaneous.
3. The use of drugs.

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1. The attitude of the physician to the patient should be one of hopefulness, truthfulness and calmness. Notwithstanding a full realization of the truth of the statement that any case of angina pectoris has within it the potentialities for coronary thrombosis, it is asserted that an attitude of confidence and hopefulness on the part of the physician, not only as to prognosis about the duration of life, but also as to the results of rational treatment, in most cases of angina pectoris is fully justified. Truthfulness on the part of the physician is absolutely essential to secure the full co-operation of the patient in the re-ordering of his life which has proved to be so necessary. To adopt an attitude of secrecy or of deception, or to assume a funereal air of

wisdom, to give a deprecating shrug of the shoulders, to fail to answer questions or to refuse adequate explanations may well prevent the physician from ever doing the patient any good. Dismissing a patient with angina pectoris with a prescription for nitroglycerin tablets to be taken when the attack comes on, and an admonition not to work too hard and to be careful in dietary measures, is not adequate therapeusis. Furthermore, the physician who hopes to be successful in the treatment of angina should not discuss the diagnosis and outline the treatment for the condition except under such circumstances as will grant plenty of time, and freedom from interruption, and that usually means at a specially appointed period and probably never during a busy office hour.

The first interview after the presumed complete examination, which should have included history, physical examination and indicated laboratory work, will often make or unmake the success of the treatment, and it is then while discussing treatment that the physician should get en rapport with his patient and learn the minutiae of what constitutes life for that particular person and the regulation of which is of such vast importance. For these reasons there should be an absence of haste on the part of the physician, and in place of haste there should be calmness, interest and deliberation, all of which tend to inspire hope for the future and make for confidence in the physician by the patient.

The measure of how much work the patient may do, or how much exercise may be indulged in, may be determined by how much is necessary to produce the attack, and advice should be given to keep the physical activities at most just below the level which usually precipitates the onset of the syndrome.

(a) Work, exercise and rest. There are certain physical tasks, however, which are better prohibited and these include shoveling snow, hurrying after trains or to keep appointments, digging or doing other laborious work in gardens or elsewhere, putting on automobile tires and chains, walking up steep hills or up long stairs, walking through deep snow or against high winds. Indulging in contests or competition should be especially prohibited, for here, in addition to the physical factor, we have added the emotional urge.

Unusual physical strain, even for a short time, may produce serious consequences especially in those who usually live sedentary lives. Fitzhugh and Hamilton[2] have shown that often unusual physical strain in those unaccustomed to it, precedes and probably bears an etiologic relationship to the onset of coronary thrombosis. It is a frequent story encountered in the middle-aged sedentary business man full of ambition on Saturday afternoon or Sunday morning, issuing forth and clearing the snow away from pathways around his home, and experiencing as the result of such effort a mild attack of angina pectoris followed within twenty-four hours by a fatal or seriously disabling attack of coronary thrombosis. Other instances of similar unusual physical tasks producing like results are familiar to physicians.

Periods of complete rest are valuable to most angina patients, but few can afford them. To those whose need is imperative, a week or two in bed at the beginning of treatment is often of value. For those persons (and they are in the largest number) who must continue working, it is of great benefit to spend the week-ends resting in bed or on a couch or just loafing around the home. Complete rest for fifteen minutes after each meal is valuable and easily carried out and it is usually possible for most patients to retire early and get rest in this manner. Special times and methods of resting will be suggested by the varying circumstances under which patients live and work.

(b) Diet, obesity and dietary habits. Probably no food per se ever induces angina pectoris and no special food should be prohibited other than those which are notoriously difficult of digestion and even then it is more of an individual peculiarity than the actual nature of the food which makes its prohibition necessary.

It is much more important to regulate the quantity than the quality of food. Many individuals may not readily digest corned beef and cabbage, but others may not readily take care of malted milk.

It is the duty of the physician to search out these idiosynerasies of the patient. It may be stated that in a general sense any food may be eaten but that meals of large quantity, irrespective of their composition, are to be avoided. At times frequent small feedings are indicated, that is, five meals of moderate quantity rather than three taken to the sense of repletion.

Most patients find the truth of these statements for themselves, and many learn that tasks may be undertaken with impunity on an empty stomach which, if attempted after a full meal, would almost surely bring on an attack of anginal pain.

Banqueting, even occasionally, should be tabooed, for it is well known that an orgy of eating or drinking is a common precedent of a disabling or even fatal coronary thrombosis.

Unless there is a special idiosynerasy to them, tea and coffee are seldom harmful.

In very elderly people a small amount of whiskey before meals and at bedtime is often helpful in reducing the number of attacks.

Tobacco, however, should be used very sparingly or omitted entirely. It is harmful in large amounts to most everyone, in moderate

amounts to many, and even in small amounts to some, and knowledge of its evil and baneful influence in the peripheral vascular diseases, such as thromboangiitis obliterans or as more familiarly known Buerger's disease, suggests that its use in angina pectoris cases is more likely to be harmful than beneficial and it is therefore probably better omitted.

The treatment of obesity is of great importance. There is probably no single therapeutic measure of such value in the treatment of angina pectoris as the reduction of obesity of marked degree, and even in those slightly overweight the reduction to normal or slightly below normal often proves an important adjunct in treatment.

The methods employed in the treatment of obesity are of importance and vary somewhat with the age of the patient.

Thyroid extract has no place in the reduction of the obesity of the usual case of angina pectoris.

In patients under sixty-five years of age, the use of a strict antifat diet is indicated and it should be known that meats red, white or black are not contraindicated in angina pectoris associated with atherosclerosis of the coronary arteries. Indeed in most people on a reduction diet the amount of protein should be definitely increased above the usual amount and better in the form of so-called red meats, else many patients during the course of reduction will suffer from languor and muscular weakness.

A diet list should be given the patient stating clearly the names of the foods allowed and prohibited and also in approximate measures the amounts of the approved foods.

To dismiss the subject of diet by giving warning to patients to be careful in dietary matters is to presume a knowledge patients do not possess. The problem of the reduction of obesity in really elderly persons differs entirely from the so-called younger group.

Very elderly people do not stand radical alterations of diet well. For some unexplained reason such changes in diet in very elderly people produce a condition of muscular and mental weakness and a diminution in energy resulting at times in such a degree of prostration as to cause the patient to become bedridden and in some cases even a fatal result may ensue from too radical changes.

In this class of cases the procedure advised is first, elimination of all fats from the diet for a period of two weeks; secondly, if this measure fails to cause steady loss of weight, reduction of the daily carbohydrate intake by twenty-five per cent is advised. In some cases the elimination of fats from the diet will result in a steady loss of weight, in other cases the additional measure of twenty-five per cent reduction of carbohydrate intake will be necessary.

However, if these two measures combined are not productive of a steady loss in weight, it is better to go no farther in the matter; for after all, moderate excessive weight in a slowly moving elderly person is not such a serious matter, and certainly not serious enough to justify such rigorous dietary restrictions as may occasionally produce a fatality.

(c) Emotional regulation. Disturbances of the emotions, although prime factors in the initiation and aggravation of angina pectoris, have not received the attention they merit and their rôle has not been sufficiently emphasized.

It is to be hoped that if this presentation makes no permanent impression on other phases of the subject matter under discussion, at least this part dealing with the disturbances of the emotions and their relationship to angina pectoris will not be readily forgotten.

It is not practical or necessary to particularize all of the various kinds of emotional disturbances which influence the course of angina pectoris, for obviously such disturbances must vary according to the nature of the individual and his environment.

Such conditions as worry about financial and business conditions, unsatisfactory domestic relationships, excessive joy, poignant grief or even pleasurable excitement are some of the common emotional disturbances. All these aforementioned emotional disturbances have been known to be factors of aggravation; and in patients in whom the response to treatment is disappointing, a searching examination which may have to include the most private parts of the patient's life should be made and will at times reveal some such cause as responsible for at least part of the anginal attacks or their unusual severity. Indeed, investigation into the business, financial, social and domestic life should be part of the examination of all cases.

Such conditions as worry over an erring son or daughter, unhappiness because of a nagging partner, fretting about disturbed family relationships, the excitement of card playing, with or without gambling, the reading of exciting literature, like the modern detective stories, the good-fellowship visits of boisterous friends, have all been aggravating factors in cases of angina pectoris.

Such emotional disturbances are of special importance in their relationship to nocturnal angina and it is of interest to note that such factors as mentioned are not always immediately operative, for it is known that the nocturnal angina may not appear until hours after the exciting cause has become latent. For instance, cases have been observed where for some reason frequent nocturnal anginal attacks occurred and the omission of the friendly game of bridge

in the evening or arguments and discussions between friends or the substitution of interesting but not exciting literature for the exciting variety has caused almost immediate cessation of the nocturnal attacks.

In some cases which do not respond to treatment the keeping of a daily diary which gives the intimate details of the patient's life may reveal a constant sequence in time between a given activity and the onset of the anginal pain. No detail is too trivial to be excluded from such a diary and it should include hours of rest and sleep, work done, exercise taken, food eaten, conversations carried on, time given to literature and other pleasant diversions.

(d) Miscellaneous.

There are certain minor habits which should be talked over with the patient. Constipation with its consequent straining at stool is dangerous and should be corrected. Anginal patients have been known to die suddenly while straining out a constipated stool.

Exposure to excessive cold even without exercise is harmful. This statement may be verified by having an anginal patient step outdoors when the temperature is around zero and even without exercise a feeling of substernal oppression will usually result.

Sun baths have no beneficial influence on angina pectoris and exposure to the excessive heat of the sun is often harmful and especially so if work or exercise is carried on during exposure to noonday sun.

Sexual intercourse, because of its intensive mental and emotional strain, is usually better omitted. The drinking of large amounts of fluid at one time is inadvisable. The patient should be instructed to take his daily fluid supply in frequent small or moderate quantities and between meals rather than with meals.

All patients with angina pectoris should be instructed that if, at any time, the anginal attack is unusually severe or long lasting and is not relieved by the usual measures, removal to the home or the hospital in the manner involving the least muscular effort is indicated and the patient should go immediately to bed and send for the doctor and the patient should also know that indigestion is not an adequate explanation of the persistence or severity of the pain.

The drug treatment between the attacks will be considered under several headings:

a. Vasodilators which include nitroglycerin, sodium nitrite, erythrol tetranitrate and possibly potassium iodide.

b. Drugs of sedation, especially bromides, phenobarbital, codein and alcohol.

c. Drugs supposed to increase the coronary circulation as theobromine sodium salicylate, aminophyllin, and theocalcin.

d. Digitalis.

a. Many drugs have been used and advised in the treatment of angina pectoris. Various opinions exist regarding the value of drug treatment and also as to the relative value of the different drugs employed.

It may be stated without fear of contradiction that no one drug is invariably beneficial. The syndrome being a subjective one, the effect of any medication has largely to be judged by the statements of the patients as to the severity and frequency of the attacks while taking a certain drug as compared with a like period during which no drug or some other drug was employed.

It is difficult at times to separate the beneficial effects derived from the reordering of the patient's life from those credited to special medication.

Notwithstanding all this difficulty, drug treatment is still employed and in some cases has seemed to prove of considerable value. Nitroglycerin given frequently during the day has been advised as a prophylactic against attacks. There is some variation of opinions as to its efficacy. Recently Brown[3] of the Beth Israel Hospital in Boston reported excellent results with this drug in the dosage of 1-500 of a grain given hourly during the day. The reported results warrant further trial of this method of administration.

Sodium nitrite and erythrol tetranitrate have not seemed efficacious and the disagreeable symptoms attendant upon their exhibition militate against their extended use. Headaches, tinnitus, disagreeable flushings, nausea and faintness have frequently accompanied their use.

Potassium iodide has not seemed of value except when treating angina associated with syphilitic aortitis.

b. Drugs of sedation are usually of great value. Before the introduction of phenobarbital, the various bromides were largely used and their value was and is often noted. The introduction of phenobarbital in the treatment of angina pectoris marked a distinct advance and there is no doubt that in the majority of cases of angina pectoris its exhibition is one of the most beneficial of all drug measures. The drug may be employed in various dosages but usually one-half a grain four times a day until sedation is obtained is adequate and then a maintenance dosage of half a grain twice a day will prove sufficient.

At times in refractory patients who could but will not take an adequate period of rest, the administration of phenobarbital in dosage of one and a half grains three or four times

a day will render such patients somnolent enough so that the rest period follows as a matter of course.

Codein is a drug of superior merit in one class of cases and in one class only. In the elderly group of anginas with marked arteriosclerosis, with or without hypertension, the exhibition of codein often results in almost complete abolition of the attacks. The picture of the elderly arteriosclerotic individual often very thin, even to scrawniness, with or without hypertension, usually showing enlargement of the heart and yet active and bustling about the business of life is a familiar one. Often such persons develop angina pectoris incident to carrying out tasks which previously were done with impunity. In such patients the administration of codein, one-eighth of a grain four times a day, is effective. After about ten days, the frequency of dosage may be reduced to twice a day and in some cases one-eighth of a grain once a day has been adequate. In a group of forty such cases followed for a considerable period thirty-six remained practically free from pain. In this same group alcohol in the form of whiskey, given in moderate doses before meals and in one larger dose at bedtime, has seemed helpful. The retiring dose given as a "hot toddy" often ensures a night of sleep, a desideratum not always easily obtained in elderly people.

c. Many drugs have been lauded as capable of increasing the coronary circulation.

In view of the permanent and probably progressive nature of the underlying organic pathologic changes present in atherosclerosis, it would seem not unreasonable to doubt the power of any drug to increase the circulation through such an atherosclerosed coronary artery. It may be that the action of this class of drugs is not well understood, for experience suggests their value in the treatment of angina.

A partial list of such drugs and combinations includes theobromine, theocalcin, theominal, aminophyllin, theobromine sodium acetate, theobromine sodium salicylate. Which of the group one may use seems to depend in many cases on which glib salesman has recently interviewed the physician and detailed him with samples of his special drug and regaled him with fanciful tales of the efficacy of the salesman's particular preparation.

It seems true that a good part of the education of our profession in therapeutics is being received from the lips of interested salesmen representing various commercial firms rather than from the teachers in our medical schools and hospitals. Whether this state of affairs redounds to the glory of our profession and the advantage of our patients is problematical.

Among the previously listed coronary artery dilators, theobromine sodium salicylate has seemed as effective as any and more so than some and it has been in use for many years in the treatment of angina pectoris. It is best given in ten to fifteen grain doses three times a day after eating and may be given in solution or in capsules. It is rather important to use the chemically pure drug.

Others of this same group of drugs may be tried and it appears at times as if alternation of two or more drugs is of value. Many of them, however, cause disturbance of the stomach if given in adequate dosage, and this should be avoided.

Aminophyllin has lately come into popular vogue. Reisman[4] of the Beth Israel Hospital noted no benefit with the usual dose, one and a half grains three or four times a day, but did find it very useful in double such dosage. Certainly the experience of others is that, with such dosage, marked nausea is very commonly experienced. Quinidine sulphate has also been credited as being of value, but due to lack of personal experience in its use no opinion of its effectiveness is offered.

d. The place of digitalis in the treatment of angina pectoris is important. Because it is the great remedy in cardiac disease, it is often administered in angina without indications for its use being present. It cannot be too strongly emphasized that routine digitalization of patients suffering with angina pectoris will result, in the very large majority of cases, in very marked increase in the number and also in the severity of attacks. This has been observed over and over again, and omission of the digitalis without any other measures being instituted has resulted in noticeable reduction in the number and the lessening of the severity of the attacks. Therefore, it should be apparent that digitalization of angina pectoris patients is not only a useless but may be a very harmful procedure. One may, therefore, establish the rule that, by and large, angina pectoris patients should not be digitalized, but like many other rules in medicine there are exceptions. Occasionally maintained digitalization may be of great benefit to an angina pectoris patient even in the absence of evidence of congestive failure. When congestive failure ensues in a patient who previously has suffered from angina, the possibility of a silent coronary thrombosis must be given consideration. Digitalization of such a patient is indicated and may be a life-saving measure and furthermore, if after digitalization there occurs complete or marked reduction in the number of anginal attacks as contrasted with the period preceding the onset of congestive failure the presence of coronary thrombosis is almost certain. Apart from this group an occasional patient may be markedly benefited by digitalization, but no rule exists

which indicates the selection of such a case prior to the use of the drug and so it may be stated that if an angina pectoris patient fails to respond to the usual methods of therapy, digitalization as an experimental measure should be used. Furthermore, the fact that the patient perhaps in previous years suffered aggravation of the angina from digitalization does not necessarily prohibit its use in later stages of the disease, for occasionally a patient exhibits an aggravation from the drug at an early stage, and yet a few years later may show benefit from its use.

COMMENT

A plan for the rational treatment of angina pectoris has been presented. This is based on a knowledge of the associated pathologic changes in the coronary arterial system, and the accompanying physiologic disturbances of cardiac musculature. It is admitted that its initiation is a time-consuming procedure but so are almost all efforts of merit. Lack of time or press of business is not an adequate excuse for failure to use it, provided the method suggested is proved to be helpful and correct. One would not accept such an excuse from a surgeon for performing an operation in a slipshod or incomplete manner. Surely the sufferings of the patient with angina pectoris are no less appealing, nor is the life of the patient with this affliction of less value than that of one ill with any of the so-called surgical diseases.

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CHAIRMAN SMITH: This paper will be discussed by Dr. Laurence D. Chapin of Springfield.

DR. LAURENCE D. CHAPIN, Springfield: *Mr. Chairman, Ladies and Gentlemen*—The hour is late. The seats are getting hard. My discussion will be brief. I have read and listened to Dr. Sproull's paper with much interest. He knows the art as well as the science of medicine. A great many cases of angina pectoris come under the care of the general practitioner and it is most important that he thoroughly understand the underlying pathology—arteriosclerosis, syphilis, diabetes, anemia, and so forth. Thanks to the postgraduate courses offered by this Society, the activities of the New England Heart Association and other aids, the average practitioner in Massachusetts does know his coronary pathology, which is the basis of successful treatment.

Dr. Sproull has limited himself this afternoon to a discussion of the anginas associated with arteriosclerosis of the coronary arteries or their branches. Much of what he has written sounds familiar in my experience and no doubt in yours. Nothing very new has developed in the treatment of angina pectoris during the past year. The reader has emphasized some of the old ideas—the avoidance of muscular strain, stairs and hills, high winds, cold air, snowdrifts, changing tires, hurried eating, exercise after meals, and so forth. Doctors subject to angina pectoris are doing these things every day. We cannot always practice what we preach.

The nitrites, the barbitals, the theophyllins are dependable. So are rest periods during the day, especially after eating. Absolute bed rest is essential if the attacks are coming too often. If this fails to relieve, total thyroidectomy is to be considered. It has given great relief in anginal failure.

The diet problem is really a very simple one: Avoid indigestion, treating each case individually; eat slowly, eat small meals, never overeat. Dr. Sproull stresses the importance of reducing weight in obese anginal cases. I like his method—low fat, moderate protein; if this restriction is not sufficient, reduce the carbohydrates 25 per cent, but go no farther. Most of these cases are over fifty years of age, and I have certainly seen harm done to the heart by cutting down carbohydrates too much.

Emotional regulation is most important. Dr. Sproull says the physician must be hopeful, truthful, calm. I would add tactful. To one patient he would not think of suggesting the possibility of coronary occlusion and perhaps later rupture of the heart, while another patient would be intrigued by a careful description of myocardial infarction and necrosis. Then too, the doctor should not interfere too much with his patient's life. The latter, thoroughly warned, may choose to step out deliberately into the danger zone, and it is his privilege to do so.

Here are a few sample admonitions which I give to angina pectoris cases:

If your bridge partner doesn't raise your demand bid, admire her corsage.

If your daughter is out on a blind date, take a grain and a half of phenobarbital.

When a member of an opposing political party is on the air, turn off the radio.

When your tax bill comes in, be nonchalant—light a cigarette.

CHAIRMAN SMITH: Is there further discussion of the paper? If not and if there is nothing further to come before the meeting, I will declare it adjourned.

[Adjourned at 5:20 p. m.]

MEDICAL PROGRESS

PROGRESS IN THE SURGERY OF THE AUTONOMIC NERVOUS SYSTEM IN 1935*

BY JAMES C. WHITE, M.D.†

I. ANATOMY AND PHYSIOLOGY

As indicated in last year's review of progress in this branch of neurology,[1] recent work has pointed with increasing emphasis to the regulation of the autonomic nervous system by groups of cells in the central grey matter along the sylvian aqueduct and in the hypothalamus. These nuclei constitute the central ganglia which control the automatic adaptations of the viscera to the external environment. They in turn are subject to a certain degree of cortical control from cells in the premotor area (Area 6 of Brodmann). Beattie[2] has written an excellent review of these investigations. There is evidence that at least three groups of efferent fibres arise from the hypothalamic nuclei. One group arises in the supra-optic area of the hypothalamus and apparently innervates the posterior and intermediate lobes of the pituitary gland; a second group from some or all of these anterior nuclei and a third from the posterior hypothalamus enter the brain stem and the spinal cord. These are the origin of the craniosacral (parasympathetic) and thoracolumbar (sympathetic) systems. According to Beattie, the hypothalamus must be regarded as the mechanism which controls the autonomic nervous system and perhaps many of the endocrine glands.

After further investigation along these lines, Ranson, Kabat, and Magoun,[3, 4] have reported their results in stimulating discrete areas of the hypothalamus in the cat with the Horsley-Clarke stereotaxic instrument. Hypothalamic stimulation often produced a picture of intense emotional excitement, with dilation of the pupils and erection of the hairs, as well as acceleration of pulse and respiration, and a rise in blood pressure. Fluoroscopic observation after a barium meal demonstrated immediate inhibition of peristalsis. Stimulation anterior to this area, in the region surrounding the anterior commissure, the septum, and preoptic area, caused contraction of the bladder, inhibition of respiration, and occasionally a drop in blood pressure, but no single centre was found to give rise to a generalized parasympathetic discharge. This lack of a single centre is not surprising in view of the discrete nature of the parasympathetic discharge. One does not, for instance, expect the pupil to constrict when the bladder contracts, whereas when the sympathetic system is aroused the entire visceral activity is influenced. These observers could not support the view held by Beattie that the tuber cinereum has parasympathetic functions, nor could they discover a sleep centre in the hypothalamus, as formerly described by Hess.

Davis, Cleveland, and Ingram[5] have done much to clear up the confusion which exists concerning the hypothalamic-pituitary mechanism. There is, as is generally known, the closest possible relation between these two structures. Topographically, they lie close together, connected by the infundibulum. As pointed out above, a clearly demarcated group of nerve fibres (*tractus hypothalamico-hypophyseus*) links the two areas, and it has also been suggested that there is a direct escape of secretion from the neurohypophysis into the third ventricle. When a tumor or experimental lesion is situated in one of these areas, the other is usually involved as well. It is therefore not surprising that the greatest confusion has existed as to which functions properly belong to the hypothalamus and which to the hypophysis. By using the Horsley-Clarke stereotaxic instrument these investigators were able to place accurate bilateral lesions in the hypothalamus without the possibility of injury to the pituitary. They found that under these circumstances complete resection of the pancreas is no longer followed by diabetes mellitus. Houssay and Biasotti had previously shown that excision of the pituitary and the elimination of its diabetogenic anterior lobe hormone produced a similar effect. Such lesions in the hypothalamus must interrupt the descending nerve fibres from the ventromedial hypothalamic nucleus. When this pathway has been transected, stimulation of the superior cervical sympathetic ganglia no longer produces hyperglycemia and glycosuria. It would therefore appear that the hypothalamus exerts a nervous control over the anterior lobe of the pituitary which is important in the regulation of carbohydrate metabolism.

An interesting insight into the control of the hypothalamus over the neurogenic-endocrine mechanisms is obtained from a case report of an angioma situated in the floor of the third ventricle, given by Davison and Selby.[6] They attribute the polydipsia and polyuria to the

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partial destruction of the paraventricular and supra-optic nuclei. The extreme subnormal temperature, which averaged between 90.6° and 96° for the last three months of life, is ascribed to extensive implication of the tuber nuclei and the mammillary bodies. There is now a considerable and convincing body of evidence to show that temperature control is a function of the hypothalamus. This patient also had a low basal metabolic rate, adiposogenital dystrophy, and hypersomnia. The pituitary gland was not involved.

Experimental hypothalamic lesions in seventeen monkeys reported by Watts and Fulton,[7] involving the supra-optic, tuber, and paraventricular nuclei, resulted in very similar symptoms of drowsiness and adiposity, as well as cardiac and gastrointestinal disturbances. The latter, reported by Hoff and Sheehan,[8] consisted of multiple hemorrhagic erosions in the gastric mucosa in five animals. There was evidence of dilation and atony of the stomach, suggesting sympathetic overactivity. In all of these animals the lesion was confined to the tuberal nuclei.

Evidence that the premotor cortex (Area 6 of Brodmann) inhibits overactivity of the hypothalamic centers has been brought forward by experimental work in the Laboratory of Physiology at Yale. Watts[9] found that faradic stimulation of many portions of the premotor area (especially the superior precentral sulcus) led to an increase in intestinal peristalsis. At times this became so active that intussusceptions were produced. In some of these experiments gastric secretion was increased. It was observed that bilateral vagotomy abolished most of the cortical responses. Watts and Fulton[10] also observed intussusception with fatal obstruction in three healthy monkeys in which the premotor area had been resected on both sides. In their experience this has never occurred following experimental lesions in other areas of the brain. They conclude that the cerebral cortex contains autonomic representation for the gastrointestinal tract which is largely restricted anatomically to the premotor area, and that this representation includes both excitatory and inhibitory components. Cortical representation of gastrointestinal activity may well explain the nausea and epigastric aura which are sometimes noticed at the onset of an epileptic attack. Cases of morbid hunger in tumors of the frontal lobes are also explainable on this basis.

Another autonomic function which has its highest representation in the premotor area is the control of body temperature. Kennard[11] has shown that a lesion limited to this area in the higher apes results in a lowering of surface temperature and diminished secretion of sweat on the contralateral side of the body. No such change results from cortical extirpations in other areas. This fall in temperature is due to an alteration in the mechanism of reflex vasodilation, since a lag in the reflex vasodilator response is noted when the animal is subjected to a rise in environmental temperature.

II. OPERATIVE METHODS

The original Royle modification of the kidney incision for resection of the lumbar sympathetic chain leaves little to be desired in its respect for anatomical structures. In children or women of delicate build it permits a most satisfactory exposure of the lumbar sympathetic chain, but in obese or heavily musceled adults it is often entirely inadequate. Since the extraperitoneal approach is both a safeguard and results in a far easier convalescence than the transperitoneal route, it should be used when a unilateral lumbar sympathectomy is to be performed. Two recent suggestions have been made to improve the exposure, both of which have overcome the difficulties of resecting the chain in the short, stocky type of individual. Harris[12] has used a transverse abdominal incision from the quadratus lumborum to the edge of the rectus sheath, cutting the oblique and transverse abdominal muscles straight across. Flothow[13] recommends a slightly oblique, muscle splitting incision at the level of the umbilicus, extending from the edge of the rectus to the quadratus lumborum muscle in the flank. The patient is placed with the side to be operated on elevated 30 to 45 degrees. The three layers of the abdominal muscles are then separated in the plane of their fibres and the peritoneum, ureter, and the abdominal contents retracted toward the midline. This gives a direct exposure of the medial edge of the psoas muscle and the sympathetic ganglionated chain which lies at the edge of the aorta or vena cava. Flothow states that the exposure is adequate for removal of the entire lumbar chain and that it is superior to any heretofore described because it permits a rapid removal of the sympathetic trunk and is without danger of hernia formation. There have been over 100 cases operated upon by the extraperitoneal approach in Flothow's clinic without a single death.

In a review of the results of sympathetic neurosurgery in England, Ross[14] brings up again the much debated problem of periarterial sympathectomy. His reports on twenty cases of gangrene in the extremities are best summarized in his own words: "It has become fashionable to say that peri-arterial neurectomy should have no place in surgery. This attitude has been adopted largely because of our inability to produce any scientific justification for the operation, but there is no doubt of its practical value in the treatment of indolent ulcers, and in al-

leviating the pain and limiting the extent of gangrene of the extremities. . . . There were 14 cases of senile gangrene. . . . Peri-arterial neurectomy of the femoral artery relieved the pain in 8 cases, the spread of gangrene was arrested in 7, and in only 7 cases was a major amputation required. Six cases of diabetic gangrene were reported. . . . Pain was relieved after periarterial neurectomy of the femoral artery in every case, the gangrenous process was arrested in 4, and in only 2 was a major amputation necessary. Whatever the explanation may be, there seems to be no doubt that this operation is of real value as a palliative measure in this painful complaint when the only alternative treatment is amputation."

In the Peripheral Vascular Clinic at the Massachusetts General Hospital this operation has seldom been used in recent years. The reason for this is that it has seemed more logical to crush the peripheral nerves in the lower leg for the relief of pain in cases of gangrene. This procedure can be counted on to give complete interruption of pain for several months, which is not uniformly true of periarterial sympathectomy. Crushing the peripheral nerves can also be counted on to produce a maximal vasodilation for over a month, which is far in excess of the transitory response which follows the periarterial operation. The results of crushing the peripheral nerves in forty-five cases of painful gangrene of the lower extremity have been reviewed recently by Smithwick and White.[15]

III. EFFECTS OF SYMPATHECTOMY ON THE CIRCULATION

The clinical importance of adrenalin and other chemical mediators in bringing about recurrent constriction of fully denervated arteries was mentioned in last year's review. Wright, Mulholland, McCloskey and CoTui,[16] have shown that the local vasoconstrictor effect of adrenalin injected under the skin in the sympathectomized leg of a dog is so intense that necrosis of the skin results. They warn against the danger of injecting this drug in the sensitized human extremity after sympathectomy. White[17] has pointed out that the satisfactory and lasting increase in blood flow which follows lumbar ganglionectomy and the far less effective results from the cervicothoracic operation can be explained by the portion of the peripheral sympathetic system which degenerates. Hampel[18] has studied the degree of adrenalin sensitization which results after degeneration of the pre- and the postganglionic set of neurones. In his experiments on the nictitating membrane of the cat he showed that the sensitization to adrenalin which develops is two- to threefold greater after postganglionic degeneration. White called attention to the classical investigation of Langley, which demonstrated that the preganglionic neurones for the arm originate in the lateral horn of the spinal cord (from the second or third to the tenth thoracic segments), traverse the anterior spinal roots, and reach the sympathetic chain over the white rami communicantes. They then run upward to terminate in the highest thoracic and lower cervical ganglia. For the lower leg and foot they originate in the ninth thoracic to second lumbar segments and run down through the lumbar ganglia to terminate in the lowest lumbar and upper three sacral ganglia. The postganglionic neurone cells are situated at the terminations of the preganglionic fibres and reach the brachial and lumbosacral plexuses over the grey rami communicantes. They are then distributed to the blood vessels of the arm and leg by the peripheral nerves. It is therefore evident that resection of the second and third lumbar ganglia causes a degeneration limited to the preganglionic neurones which mediate vasoconstriction in the foot, since the postganglionic neurones to the sciatic nerve originate at lower segments. In the upper extremity, however, resection of the inferior cervical and upper two thoracic ganglia results in the degeneration of the entire postganglionic network. As a result of these two physiologically different operations, sensitization to adrenalin is maximal in the hand, minimal in the foot.

Clinically this offers a satisfactory explanation for the mediocre and the excellent results after the standard operations which have been developed in the past thirteen years for Raynaud's disease of the upper and lower extremities respectively. The experimental observations on which this theory is based have been thoroughly confirmed by Grant.[19] Modification of the technic for upper extremity sympathectomy to interrupt only the preganglionic portion of the peripheral vasoconstrictor pathway by Smithwick at the Massachusetts General Hospital and by Telford[20] in England is resulting in a striking clinical improvement. After this more physiological type of operation it is no longer possible to induce postoperative cyanosis in the hands by exposure to cold or nervousness, and the results up to a year and a half have been as good as those commonly seen in the lower extremity.

The clinical results of sympathectomy in England for vasospastic disorders have been summarized by Ross.[14] Reviewing the results submitted to him by the Fellows of the British Association of Surgeons, he found that:—

In Raynaud's disease (sixty-one cases), cervicothoracic ganglionectomy produced "a great diminution in the frequency and severity of attacks, but not complete absence of attacks" in thirty cases. When the condition was present in a severe form and complicated by sclero-

derma, the operation was a complete failure in eight out of eleven cases. In the feet there was only one late failure after twenty lumbar ganglionectomies. This occurred in a severe case complicated by ulceration. These statistics bring out very clearly the difference described above in the relative effectiveness of cervicothoracic and lumbar ganglionectomy.

In circulatory disorders following infantile paralysis resulting in coldness, cyanosis, and ulceration of the legs, lumbar ganglionectomy gave a worth-while increase in circulation in twenty-three out of twenty-six cases. One case was reported in which lumbar ganglionectomy was without effect on the trophic ulcerations of spina bifida.

In thromboangiitis obliterans the beneficial effects of sympathectomy seem to depend upon the possibility of dilation of the peripheral vessels as yet unaffected by the disease. This gives the all-important collateral circulation a chance to develop. It is questionable whether the pathologic process is retarded by the operation, and there is no doubt that serious complications of the disease can appear very shortly after operation. In two of the reported cases amputation had to be undertaken because of popliteal thrombosis which took place within a week of the patient's discharge from the hospital. In twenty-nine cases of intermittent claudication a notable increase in walking ability took place in nineteen. Rest pain was relieved in twelve out of fifteen cases. In twenty-two cases complicated by gangrene of the toes, fourteen were arrested, but eight required a major amputation. Two out of three cases of the disease in the arm were benefited by cervicothoracic ganglionectomy.

Bird[21] has called attention to the value of sympathectomy or sympathetic block when an important artery must be divided or has been suddenly occluded. He performed a lumbar ganglionectomy four weeks prior to an obliterative aneurysmorrhaphy on the popliteal artery and records a most satisfactory state of the circulation after the operation.*

Sympathectomy as a cure for the extreme and disabling forms of hyperhidrosis in the extremities is becoming a recognized procedure. The most interesting report on this condition is that published by Adson, Craig, and Brown,[22] who describe five successful cases. They comment on the fact that this excessive form of sweating occurs in the asthenic type of individual. Besides showing various forms of vasomotor instability, these patients are prone to have functional disorders of the gastrointestinal tract, fatigued states, and vasomotor rhinitis. The conception that this condition originates in higher centers is strengthened by the report of a boy who during his waking hours would develop drenching sweats and a fall of body temperature to as low as 91°. Sleep and amytal anesthesia controlled the central irritability with a disappearance of hyperhidrosis and a return of normal temperature. The probable etiologic factor was encephalitis.

A new and somewhat questionable application of cervical sympathectomy has been reported for the treatment of retinitis pigmentosa. In this type of progressive blindness there is a striking pigmentary degeneration and narrowing of the retinal vessels. Although it is well known that cervical sympathectomy produces a definite and lasting dilation of the vessels in the normal retina, this is unlikely to occur in a condition where they are compressed by gliosis of the retina. Walsh and Sloan[23] have reported three cases with failure in two and "a possible slight benefit" in the third. They state specifically that ophthalmoscopic examination failed to show increased size of the retinal arteries. After operation on six cases, de Takáts and Gifford[24] found that in no case was there an improvement in the acuity of vision or in the visual fields. In two out of four cases MacDonald and McKenzie[25] report only slight improvement, but conclude with the hope that advancing loss of vision may be held in check by the operation. Kerr,[26] who has published the most successful series, reports improvement in only three out of eight cases.

The experimental work of Heymans and his colleagues on the regulation of cardiovascular tone by the carotid sinus, which was reported in last year's review,[1] has led to the description of a most interesting clinical syndrome by Ferris, Capps, and Weiss.[27] This study is based on observations on thirty-two patients who suffered from spontaneous attacks of dizziness, weakness, and unconsciousness, with or without convulsions, and in whom mechanical stimulation of the neck over the carotid bifurcation promptly induced manifestations of identical nature. The evidence indicates that these attacks depend on hyperactivity of the carotid sinus reflex. Depending on the efferent pathway involved, three types of syncope and convulsions have been described: (a) the type depending on inhibition of heart rate; (b) the type depending on a fall in arterial pressure; (c) the "cerebral type" in which changes in neither heart rate nor blood pressure plays a rôle. Type (a) is purely a vagal reflex and can be abolished by atropin. The cerebral type, however, is uninfluenced by drugs. It is interesting that, as in epileptic fits, the convulsions are not accompanied by a generalized anoxemia

*At the Massachusetts General Hospital we have had a similar satisfactory experience with paravertebral lumbar novocain and alcohol injection in a case of embolism of the iliac artery. We have been intending to use the same procedure when it becomes necessary to ligate the carotid or subclavian artery. The value of alcohol by mouth as a vasodilator should be kept in mind for use in acute arterial occlusions when the patient is far from a hospital.

of the brain, although local areas of cerebral vasoconstriction may occur. The sensitive carotid sinus has been surgically denervated in seven cases with a complete cure of spontaneous attacks to date in every case.

IV. EFFECTS OF SYMPATHECTOMY ON HYPERTENSION

A widespread interest in surgical attempts to lower states of excessive hypertension began in this country in 1934. Although the mechanism underlying essential hypertension is unknown, a neurogenic factor is probable because these subjects characteristically show excessive vasoconstrictor responses to cold and emotion. Hypertensives in the earlier stages of the disease, who show this lability of blood pressure, who are under fifty years of age, and free from marked retinal and kidney damage, constitute the most favorable group for operation. Three types of procedure have been attempted at the Mayo Clinic and the results discussed by Brown, Craig, and Adson[28] and by Adson.[29]

1. Although favorable reports have been published on subtotal resection of the adrenal glands, a review of their experience on thirty-two cases indicates that nerve section is a more effective and less dangerous procedure. Adson reports a case, where an adrenal cortical tumor was suspected, and from which he removed the right adrenal and about three-fifths of the left. The patient developed mild adrenal insufficiency, but without any effect on the blood pressure.

2. Subphrenic resection of the splanchnic nerves was performed in seven cases, but without a significant reduction of blood pressure. Adson has recently enlarged the scope of this operation by resecting the twelfth rib. The improved exposure is enabling him to remove a large part of the celiac plexus and the upper two lumbar ganglia, as well as the splanchnic trunks. He is most optimistic concerning the possibilities of this new method.

3. Ventral rhizotomy, from the sixth thoracic to the second lumbar segments, results in a sympathetic denervation of all the arteries below the diaphragm (75 per cent of the total vascular bed), the kidneys and adrenal glands, as well as in a reduction of intra-abdominal tension by relaxation of the abdominal wall. A series of twenty-two of these operations are reported by Adson. Excellent clinical effects, with sustained lower levels of blood pressure, resulted in nine. Only fair results were obtained in six cases, whereas three patients failed to obtain relief and two died following the operation. In two patients operation had been performed too recently to draw any conclusions. The fact that Adson is shifting his attack to a more extensive neurectomy beneath the diaphragm coincides with the more conservative opinion that spinal root section is probably too radical and mutilating a procedure. Nevertheless, Heuer[30] has continued to advocate rhizotomy with considerable enthusiasm and a good number of really striking results. Out of a series of nine severe hypertensives, two have maintained a pressure of 124/92 and 122/80 for over three months, and in three others the blood pressures have remained below 145/100. One patient was not improved and another died at the end of the operation. The other two were followed for only a month.

Peet,[31] who has had by far the largest experience with the surgical treatment of hypertension, has advocated a transthoracic but extrapleural resection of the splanchnic nerves above the diaphragm. He performs this operation bilaterally and usually at a single stage, resecting a short length of the tenth rib and retracting the pleura laterally off the sides of the lower thoracic vertebrae. This enables him to remove the lower portion of the ganglionated chain and a 10 cm. length of the major, minor, and least splanchnic nerves. This operation is less likely to miss important connections or to be followed by nerve regeneration than the approach beneath the diaphragm, but Adson's modification of the latter procedure has the advantage of interrupting vasoconstrictor impulses to the legs as well as to the abdominal viscera. Peet has operated on over sixty severe hypertensives (systolic pressure over 200 mm.) and has limited his selection only to patients below fifty and free from a significant degree of renal damage. There have been three operative deaths. Forty patients have been checked from two to eighteen months postoperatively. Six (15 per cent) are symptom-free and maintain a normal pressure suggesting permanent cure. Fifteen (37 per cent) show an appreciable drop in pressure with symptomatic improvement. Of the nineteen (48 per cent) showing no fall, many have improved symptomatically, especially in regard to headache.

The discrepancy in operative results and the different methods being employed make it obvious that no dogmatic views can be hazarded as yet concerning the ultimate value of these procedures. The invariably unfavorable prognosis of the severe forms of hypertension does, however, justify a certain degree of careful surgical experimentation. It seems as though this particular problem cannot be settled in the laboratory. Considering that the clinical evidence reviewed above is as encouraging as it is, further reports of prolonged postoperative observations will be watched with the keenest interest.

V. SYMPATHECTOMY FOR VISCERAL PAIN

In discussing the effect of sympathectomy on pain it is always important to emphasize that, strictly speaking, the sympathetic is purely a motor system to control and correlate visceral activity. However, somatic sensory fibres, identical with those which run in purely sensory nerves to the skin, are found in all the important nerves to the viscera. One seeming exception is that no afferent fibres run in the upper portion of the cervical sympathetic trunk. It is, therefore, hard to explain why cervical sympathectomy should be of value in the relief of migrainous headaches. Several years ago Dandy reported two successful results from this procedure, and Craig[32] has reported two further instances. In each case, where all other measures had failed, cervicothoracic ganglionectomy has resulted in complete relief lasting from four to fifteen months. The benefit, however, was not immediate, but resulted in a rapid diminution of the severity of headaches. It is therefore evident that the effect was not due to an interruption of sensory pathways, but to some influence on the motor mechanism of the attacks.

In their experiments on cardiac pain, in which they injected twenty per cent lactic acid into the coronary arteries after decerebration, Moore and Singleton[33] found that pain reactions were constantly present as long as the thoracic sympathetic chains remained intact. In contrast to this, resection of the upper thoracic ganglia on one side (stellate to seventh thoracic) uniformly prevented any signs of discomfort following the injection of the corresponding coronary artery. These clear-cut experiments indicate that pain fibres ending in the region of either coronary artery reach the spinal cord by way of the ipsilateral rami of the upper thoracic sympathetic ganglia. The authors also showed that removal of the cervical sympathetic trunks and vagotomy were without effect. They therefore concluded that, if this scheme of innervation in cats applies to man, resection or injection of the upper thoracic portion of the ipsilateral sympathetic chain should be the operation of choice for coronary pain.

Mandl,[34] who originally advocated paravertebral injections for cardiac pain, has published statistics of the results of his alcoholic injections for angina pectoris and other forms of visceral pain. In a series of fifty cases there have been no serious complications. He has obtained favorable and lasting relief of angina pectoris in 50 per cent of his cases.

In an impartial evaluation of the two outstanding methods for the surgical treatment of angina pectoris, Marvin[35] has compared the results of paravertebral alcohol injection with those of total thyroidectomy. He states that "the percentage of relief following alcohol injections is higher than that following thyroidectomy. . . . Further advantages of this procedure are the absence of operative mortality, the absence of any permanent ill-effects, the short period of hospitalization (usually three or four days as compared with several weeks for thyroidectomy), and the possibility that other methods may be tried in case of failure, without the patient's condition having been altered for the worse. The disadvantages . . . are chiefly three: the technical difficulty of injecting the alcohol accurately, the neuritis that follows it, and the fact that relief is strictly limited to the side on which injection is performed." Speaking of total thyroidectomy, Marvin points out that: "The disadvantages are numerous; they include operative and postoperative death, recurrent laryngeal nerve paralysis, parathyroid insufficiency, and myxoedema."

The most recently published statistics on the results of paravertebral alcohol injection for angina pectoris from the Massachusetts General Hospital[36] are as follows: Thirty-six patients with intractable angina pectoris have been injected. Of these, 67.7 per cent have been relieved (on the side injected), an additional 17.6 per cent have been reduced from the severest form of the disease to mild infrequent attacks which are easily controlled by nitrites. Only 14.7 per cent have failed to secure relief, all of these falling in the first half of the series. There has been no failure after a satisfactory alcohol block and only one early death which could possibly be attributed to the injection (probably a coincident painless coronary occlusion). Recent improvements in the technic of injection[17] have greatly reduced the ensuing intercostal neuritis, which has constituted the single drawback to this valuable procedure.

Another type of sympathetic intervention for visceral pain which has been extensively discussed in the past year is presacral neurectomy. Pemberton[37] has reported fifteen operations for essential dysmenorrhea in which a cervical dilatation and an Olshausen suspension were performed in addition to the presacral neurectomy. This makes it difficult to judge the specific value of the neurectomy per se, but twelve were relieved, one was considerably benefited, and two obtained no improvement. The author states that dilatation and suspension relieve about 65 per cent, so that the addition of the neurectomy is a distinct benefit. He also advocates this form of neurectomy as an adjunct in the treatment of dysmenorrhea associated with pathologic conditions such as chronic pelvic inflammation, painful fibroids, and prolapse. In advanced cancer of the cervix Pemberton failed to secure improvement in four cases. Counseller[38] reports that presacral neurectomy has given satisfactory results in 90 per cent of the cases

at the Mayo Clinic. The operation is not followed by any deleterious effect in the female and normal parturition has followed on numerous occasions. Behney[39] has performed presacral neurectomy on twenty-two patients with incurable carcinoma of the cervix uteri. All of these women had received intensive radiation therapy, but continued to suffer excruciating pain in the lower abdomen, sacral region, and even in the thighs. When pain could not be palliated and x-rays of the pelvic girdle revealed no bone invasion, the superior hypogastric plexus was resected from the inferior mesenteric artery down to the uterosacral ligaments. While Behney states that this operation will not affect pain due either to ureteral obstruction or to bone metastases, it relieved 72 per cent of his selected cases. The immediate operative mortality was 14 per cent, but seven of the cases lived less than four weeks after the operation. Bladder pain, unfortunately, is not equally susceptible to relief by presacral neurectomy, because many afferent fibres enter the sacral nerves.

VI. EFFECTS OF SYMPATHECTOMY ON VISCERAL MOTOR INNERVATION

In continuation of an interesting series of experiments which were published in 1934, Knight[40] has given further evidence of the relationship of sympathetic tone to achalasia of the cardiac sphincter. By stimulation experiments in cats he has shown that the interdiaphragmatic and intra-abdominal portions of the esophagus function as a true intrinsic sphincter which is relaxed by the vagus and contracts on sympathetic stimulation. The sphincter receives its sympathetic supply from the celiac plexus in fibres which follow the course of the left gastric artery and its esophageal branch to the lower end of the esophagus. Excision of the extrinsic nerves supplying the esophagus showed that vagal section produced achalasia of the cardia. If, however, both thoracic sympathetic chains were excised at the same time, no obstruction resulted at the cardia. After achalasia had been produced by vagotomy, subsequent celiac sympathectomy resulted in complete relief. Knight divides esophageal obstruction in man into: (1) cases of vagus failure—achalasia; (2) cases of spasmodic contraction — cardiospasm; (3) hypertrophic stenosis of the cardia. The first two result from autonomic imbalance in the control of the cardia and can be improved by sympathectomy. Knight and Adamson[41] report six cases in which achalasia was relieved by excision of the left gastric artery with its surrounding fat and nervous tissue.

After investigation of the nervous control of defecation, Denny-Brown and Graeme Robertson[42] have emphasized the importance of intrinsic reflexes which are active after injuries to the lumbar and sacral portions of the spinal cord. Under these circumstances distention causes contraction of the rectum with reciprocal relaxation of the anus. When the sacral cord segments are intact, spinal reflexes bring a greater fusion of rectal contractions with a consequent more massive and complete defecation. As in the case of their previous work on the bladder, these investigators state that the sympathetic nerves (hypogastric) to the rectum and anus are no part of the nervous mechanism essential to evacuation. The mechanism of defecation, provided delivery of fecal material from the colon is adequate, depends primarily upon the reaction of the rectum to distention. Woollard[43] has reached a very similar conclusion, as he holds that the concept of sympathetic inhibition of bowel tone and tightening of the internal sphincter, with opposite effects on the part of the sacral nerves, is an oversimplification of the problem.

Trumble[44] in experiments on dogs and monkeys arrived at somewhat different conclusions, as he often observed inhibitory effects upon the colon on stimulating the lumbar sympathetic nerves. He calls attention to the fact that peristalsis is always inhibited in the course of laparotomy, unless these nerves are blocked by spinal anesthesia. On stimulation of the pelvic parasympathetic nerves he observed quite constantly that the colon and rectum were shortened and drawn down toward the pelvis. Furthermore, after degenerative section of the pelvic nerves, dogs do not store feces, but pass numerous small masses throughout the day and night. Storage and mass evacuation are abolished, and the inherent peristaltic mechanism of the alimentary canal, previously kept under control by the pelvic nerves, comes to the fore and material is passed as it becomes available. This type of defecation is seen clinically in the frequent small stools which are passed involuntarily after injuries to the spinal cord and in patients with colostomies. Trumble's observations of inhibition of peristalsis in the colon on sympathetic stimulation and its increased activity in the course of laparotomy when these nerves are blocked, may explain the favorable results of sympathectomy in megacolon, as this procedure partly releases the intrinsic neuromuscular mechanism (described by Denny-Brown and Graeme Robertson) from abnormal interference of higher reflexes. The excellent results of this operation are best brought out in Ross's[14] collected statistics. Of twenty-nine cases of Hirschsprung's disease in children, twenty-one are reported as completely successful, seven as improved, and only one as being a failure. Many of these were followed for over two years. Ross reports distinctly inferior results in the acquired form of intestinal stasis

in adults. In a series of fifteen cases, only four were successful, four were improved, and seven failed to obtain any benefit.

Ross[14] reports several good results of sympathectomy in cases of bladder dysfunction associated with megacolon, but attempts to relieve bladder paralysis by presacral neurectomy (section of the sympathetic "bladder filling" nerves) have been so discouraging that reports of this procedure have disappeared from the literature. Under the most favorable circumstances satisfactory emptying of the bladder can be mediated by the intrinsic reflex mechanism. This, however, is less effective than in the passage of feces. When it is ineffective with a large amount of residual urine and chronic infection, presacral neurectomy offers little hope of re-establishing normal micturition. In experiments on dogs and cats Creevy[45] and McCaughan and Hershey[46] have shown that section of the hypogastric nerves produces only a slight transitory increase in the frequency of micturition. When the bladder is severely damaged by cutting the pelvic nerves, additional section of the hypogastric fibres produces no change. In recent and unpublished cystometric observations on human beings after presacral neurectomy, Munro has noticed no alteration in the behavior of the bladder.

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CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 22361

PRESENTATION OF CASE

First Admission. A fifty-three year old American motorcyclist entered complaining of left flank pain.

Eight weeks before admission he experienced a rather sharp pain in the left groin which worked its way up into the left flank. At the same time he had chills and fever frequently throughout his illness. For the first six weeks the pain was a persistent dull ache, but occasionally was very sharp. It was not radiating but was aggravated by moving, coughing and deep inspiration. During the past two weeks there was a visible, acutely tender swelling in the left flank. He had lost twenty-six pounds in weight during this illness.

His mother died of carcinoma of the cervix. His first wife died of tuberculosis thirty years before admission. His second marriage occurred fourteen years later. He had one child living and well.

His past history is noncontributory, except that two months before his present illness a boil over the lumbar spine was incised by a physician. This healed well.

Physical examination showed a well-developed and poorly nourished man who moved about with his spine erect. The neck was not stiff. Examination of the right chest was negative. The lower half of the left chest posteriorly was dull. This dulness merged with that of a tumor in the left flank. The latter was described as an inverted, bowl-like, fluctuant, tender mass approximately 5 centimeters in diameter. When the patient coughed the impulse was transmitted into the mass. Above this area, at about the angle of the scapula, were a few coarse râles. The heart was not enlarged. No murmurs were heard. The blood pressure was 110/60.

The temperature was 99.3°, the pulse 92. The respirations were 32.

Examination of the urine was negative. The blood showed a red cell count of 3,070,000, with a hemoglobin of 60 per cent. The white cell count was 13,200.

X-ray examination of the spine showed slight arthritic changes but was otherwise negative. Examination of the urinary tract showed that the kidney outlines were normal in shape and position on both sides. The right was considerably larger than the left.

In the Emergency Ward odorless, thick, greenish gray, purulent material was aspirated from the left flank mass. A smear showed gram-positive diplococci. The following day an oblique incision, about 8 centimeters in length, was made over the mass just below the last rib. A very large abscess cavity was immediately entered which contained thick pus and a good deal of free gas. The cavity extended upward under the twelfth rib and led to an abscess in the left paravertebral region, extending up almost to the scapula. A large-sized chest tube was sewed into the cavity and brought out through the wound at the lower end.

A chest film taken on the sixth postoperative day showed dulness in the lower part of the left chest. The shadow was rather faint, roughly triangular in shape with its apex toward the hilus and the base on the axillary border. The costophrenic sinus on this side was obliterated. The outline of the diaphragm was distinctly seen but was higher on the left than on the right.

He did fairly well and was discharged three weeks after operation. At that time the cavity had a capacity of 10 cubic centimeters and there was probably a bronchial fistula.

Second Admission, two years later.

His wound had healed well and he had no complaints until about nine months before entry when he began to spit up small amounts of blood every day. Associated with this was the gradual onset of pain, wheezing, hoarseness and exaggeration of his shortness of breath which he had noticed upon exertion during the past two years. The pain was dull, but at times was sharp and knife-like, occasionally radiating down along the costal margin and often to the back. It was aggravated by lying flat but not by coughing. For the past six months he had frequent attacks of nocturnal dyspnea. His physician sent a specimen of his sputum to a laboratory and it was reported as negative for tuberculosis.

Physical examination showed a rather obese middle-aged man in no acute distress, occasionally coughing up bloody sputum. His voice was hoarse. The right chest was negative. The left upper lobe anteriorly showed dulness, absent tactile fremitus and voice sounds, and diminished breath sounds. Expiration was prolonged. Inspiration was wheezing and "crowing". Posteriorly, the upper half of the left lung field was dull and had diminished breath sounds, voice sounds and tactile fremitus, with occasional râles. The base was also dull and no sounds could be heard. The heart was not remarkable except for a soft apical systolic murmur. The blood pressure was 140/80. The

liver edge was felt three fingerbreadths below the costal margin. There was early clubbing of the fingers.

The temperature was 99.8°, the pulse 100. The respirations were 24.

Examination of the urine was negative. The blood showed a red cell count of 5,060,000, with a hemoglobin of 75 per cent. The white cell count was 15,000, 74 per cent polymorphonuclears. The sputum was mucopurulent and bloody. A smear showed numerous gram-positive cocci and bacilli. The stools were negative. A Hinton test was negative.

A film taken six weeks before admission in the Out-Patient Department showed homogeneous dulness in the region of the left upper lobe, in the center of which were ring-like shadows of decreased density, very suggestive of a cavity but without any definite fluid level. There was also an increase in the dulness previously described at his first admission. The heart and mediastinum were pulled somewhat to the left. There was a definite elevation of the left bronchus and a bulge in the region of the pulmonary conus. The entire left chest was smaller than the right. An oblique view showed thickened pleura. The findings were those of an incomplete atelectasis of the left upper and lower lobes with a probable area of destruction within the upper lobe. A gastrointestinal series showed no evidence of intrinsic disease of the esophagus, stomach or duodenum.

Bronchoscopic examination showed complete obstruction at the left lower lobe bronchus and partial obstruction to the left upper lobe. No tumor mass, outcropping or hemorrhagic area could be seen. The obstruction seemed to be entirely peribronchial thickening.

Three weeks after admission an exploratory thoracotomy was performed. He did poorly postoperatively and died three days later.

Differential Diagnosis

Dr. F. Dennette Adams: Infection is certainly indicated by the history on the first admission. In many cases it is important to distinguish between the true chill and the chilly sensations which accompany the onset and occur during the course of certain specific infections, but the distinction is not made in this case.

The cough and yellow sputum suggest disease of the lungs or pleural cavity; pain, aggravated by cough, moving, or deep breathing, is also often characteristic of pleural involvement. However, one rarely finds the pain of pleurisy actually in the flank; it is usually higher and farther forward. Other types of pain—that referred from disease of the spine, or spasm of the back muscles, for example—are usually aggravated by very much the same movements.

The appearance of swelling in the left flank probably indicates a collection of pus. Whence has it originated? There are several possibilities. This patient could conceivably have had pneumonia followed by empyema, and the picture on admission could have been that of empyema necessitatis: a spontaneous breaking through of the pus toward the surface. We have nothing in the history, however, to point toward previous pneumonia. Furthermore, empyema necessitatis usually appears anteriorly. Tuberculosis is suggested by the fact that the patient's first wife died of it: intimate exposure is established. Sources of pus in this disease could be a cold abscess of a rib, but this is usually a much less acute process, or it could be pyopneumothorax, which is, however, only a remote possibility. Pneumothorax usually begins suddenly, with acute dyspnea, pain in the chest, probably collapse; and pus, once formed, would be apt to drain through the hole in the lung rather than burrow a new passageway to the surface.

A much more likely answer to our question than any of these is that deduced from the relation that the collection of pus may bear to the abscess of the back which had been opened two months previously. That incision may have provided inadequate drainage and if such were the case it is conceivable that the infection worked inward, spread upward under the diaphragm, and entered the pleural cavity by extension through the diaphragm.

Even more likely is the possibility that an embolic focus started in the lung or pleura and produced pus in the left pleural cavity which extended downward through the diaphragm.

Acute severe infection with, doubtless, dehydration is a plausible explanation of the marked loss of weight.

The description "moving with the spine erect" probably means moving with the spine held in a rigid posture. This is a protective mechanism traceable to irritation of the back muscles, probably the erector spinae group.

The lung findings are not completely reported. Perhaps there was so much edema of the soft tissues that breath sounds in the affected region could not be heard. The presence of impulse on cough does not necessarily point to direct connection of the abscess with the pleural cavity. Downward motion of the diaphragm might produce it, even if all the pus were below this structure.

The first series of x-rays was noncontributory, except for excluding a large infected kidney. Considering the history and physical examination, such a possibility would not seriously have been entertained. X-ray would not necessarily exclude perinephric abscess, which would be more likely than actual disease of the kidney.

The report of the operation does not make it clear whether the pleural cavity was actually entered. Surgical entrance must have been ef-

fected below the level of the diaphragm, but if the cavity was found to extend as high as the scapula one could assume that the pleural cavity must have been entered. However, if such were the case, x-rays six days later would be expected to show a partial pneumothorax with partial collapse of the lung on the affected side. So it might be possible that the pus was entirely outside the pleural cavity. On the other hand, x-ray showed that the costophrenic angle was dull, a decided factor in favor of pleural cavity involvement.

The presence of gas is hard to explain. Foul smelling pus, with gas, due to an anaerobic streptococcus is sometimes found in empyema following certain atypical cases of pneumonia not due to the pneumococcus. Colon bacilli, a common cause of gas, were not reported. Possibly a culture would have shown them. Air from the lungs through a fistula seems unlikely.

A PHYSICIAN: Could it not have been a bronchial fistula?

DR. ADAMS: Then there should have been more signs in the chest cavity; and the man would have been coughing up more pus than the history indicates.

I do not know what evidence there might have been of probable bronchial fistula. Its presence could have been determined definitely by injecting a small amount of Dakin's solution or some similar preparation into the cavity. If a fistula existed, a sufficient amount of the liquid would have found its way through the fistula to enable the patient to smell or taste it. Demonstration of its existence in this case would help to determine whether the abscess found at operation did or did not extend into the pleural cavity.

A PHYSICIAN: It would have been easy enough with lipiodol.

DR. ADAMS: Yes, it probably would have; but the test just mentioned does not require another x-ray.

It is impossible to decide on the basis of the evidence at hand how the abscess originated; or whether it existed above or below the diaphragm, or both. My conjecture is that it started below the diaphragm and extended upward into the pleural cavity, but it could just as well have started in the chest from an embolic focus and worked downward.

On his second admission this patient had a new series of complaints. Barring local lesions in the nose or throat, the most common causes of hemoptysis are tuberculosis, bronchiectasis or lung abscess, and congestive heart failure; of the heart lesions, mitral stenosis is the most frequent. Aneurysm and mediastinal, lung, or bronchial tumor should also be considered, but these are not seen so often. The history is not inconsistent with any of the aforementioned, but points toward none of them in particular. Wheezing, hoarseness and pain are not common with mitral disease; they suggest, rather, bronchopulmonary or mediastinal disease.

Physical examination points definitely toward disease involving the left upper lobe. Three possibilities are to be considered: (1) tuberculosis, (2) some process related to the previous infection, and (3) tumor.

It is hard to believe that he could have tuberculosis sufficient to give the symptoms and signs described without more evidence of systemic reaction. Tuberculosis does not usually cause bronchial obstruction. He is well nourished; apparently he has not been losing weight; and there is no history of weakness, fever, or the other common symptoms of advanced tuberculosis. Furthermore, there was, at the previous admission, no evidence of tuberculosis.

Assuming, as we do, that he had trouble with the lung previously, it is natural to consider seriously the extension or recrudescence of this trouble as the cause of this present difficulty. This dulness, absent tactile fremitus, and the character of the breath sounds can be satisfactorily explained on the basis of an old chronic infectious process in the lung, probably with bronchiectatic abscess and marked thickening of the pleura. Obviously, air is not going into the upper lobe in normal fashion. The lower lobe findings are probably due to thickened pleura, the result of the former damage in this area. Bleeding, as indicated earlier, is common with bronchiectasis or abscess. Hoarseness, however, is difficult to explain on this basis.

Tumor could give a similar picture with infiltration of the lung and, probably, block to the passage of air in a large bronchus. Hoarseness would then be accounted for by pressure on the recurrent laryngeal nerve. Clubbing of the fingers is seen with any of the usual chronic lung conditions, most commonly with abscess or bronchiectasis.

The presumable enlargement of the liver is difficult to explain unless on the basis of metastatic malignant disease.

The laboratory findings are not helpful. With malignant disease of nine months' duration or with chronic infection, one would hardly expect the red count to be as high as 5,000,000.

The x-ray report seems to localize the condition to the left lung, chiefly the upper lobe, but does not clarify the problem. There is, obviously, contraction due to pleuritis, with pulling of the mediastinum toward the left. There is evidence of bronchiectasis or abscess in the left upper lobe and an area of density around it due, likely, to pulmonary infiltration. Scar tissue contraction could reduce bronchial caliber and give rise to the atelectasis.

On the other hand, cancer of the lung, which

has broken down, could give a similar picture and would be more apt to cause bronchial obstruction.

Bronchoscopic examination provided no added information, except for showing bronchial block and excluding tumor in the lumen of the bronchus.

I do not believe there could be complete obstruction, otherwise the purulent sputum arising in the abscessed region would not be coming through.

The diagnosis in this case is very difficult. The patient appears to have had empyema and abscess in the retroperitoneal region two years ago. Now he returns to the hospital with a destructive lesion in the left upper lobe. My inclination is to adhere to the principle of not making two diagnoses where one may suffice. I believe that the recent process is related to the older; that he has developed a slowly progressing, nontuberculous infectious process in the left upper lobe, with destruction of the lung tissue, with contraction due to scar formation, and with abscess or bronchiectasis. However, it is impossible to exclude cancer with secondary abscess, and I would not be surprised if Dr. Mallory reports this as the postmortem diagnosis.

DR. TRACY B. MALLORY: With upward extension of infection, would you not expect to find the most advanced lesion in the lower rather than in the upper lobe?

DR. ADAMS: Yes, unless it has slowly spread to the upper lobe.

CLINICAL DIAGNOSIS

Carcinoma of the bronchus, left.

DR. F. DENNETTE ADAMS' DIAGNOSES

Chronic infectious process of the left lung with abscess formation.
Chronic pleuritis.
Cancer of the lung?

ANATOMIC DIAGNOSES

Epidermoid carcinoma of the lung with metastases to the bronchial and mesenteric lymph nodes, and with erosion of the pulmonary artery.
Hemorrhage into the bronchial tree.
Pulmonary abscess.
Pleuritis, fibro-fibrinous, left, marked.
Arteriosclerosis: Pulmonary artery, marked; aortic and coronary, slight.
Operative wound: Exploratory thoracotomy.

PATHOLOGIC DISCUSSION

DR. MALLORY: What we found was a combination of cancer and abscess. There was a cancerous infiltration of the bronchus leading to the left upper lobe which almost completely occluded the lumen. There was still a very narrow air passage left, however, down the center. The entire lung beyond that was a mass of necrotic cancer with numerous pus-filled cavities. That is a very common combination since the moment you begin to get bronchial obstruction the likelihood of infection beyond the point of the obstruction becomes very great. In a great many of these cases of cancer of the lung it is the infection beyond the cancer that causes all the symptoms rather than the cancer itself. I think that was probably more or less true here.

The lower lobe was somewhat atelectatic but otherwise negative. The right lung showed a moderate grade of compensatory emphysema. The entire pleural cavity on the left was obliterated by old fibrous tissue. I cannot make any accurate guess as to how long it had been obliterated. We found nothing in the abdominal cavity to explain his previous abscess and draining sinus and the scar so far as we could make out seemed to lead up to the pleural cavity. It seems reasonable to conclude he had empyema entirely unconnected with the present illness which nearly drained itself, the surgeon finally aiding with an incision through the skin. There were no metastases at all. A good many of these lung cancers metastasize very early and, as you probably know, they have some very characteristic sites for metastases. The brain is a particularly common one and the largest series of cases of cancer of the lung that has been reported in this country came from Cushing's clinic in the Brigham Hospital. In most of the cases of cerebral metastasis the first symptom was that of brain tumor. Another place that we have found metastases with remarkable regularity has been in the adrenals; metastases to both adrenals are very common with pulmonary cancers. I think it is perhaps fair to assume that the sepsis killed him too soon to give a chance for metastasis.

Of course one way of making an absolutely positive diagnosis in this sort of case is to obtain a specimen by bronchoscope which shows tumor. Until you do that you can never do more than guess, but where there is no obvious tumor mass projecting up the bronchus the bronchoscopist may not be able to get a specimen. Speaking from considerable practical experience, the piece of tissue that the bronchoscopist is able to get is frequently so extremely minute that the pathologist may not be able to make the diagnosis anyway. A negative bronchoscopy is of little significance as compared with a positive one because the bronchoscopist may not pick his material from the right spot, and may not have obtained enough to give the pathologist a fair chance to make a diagnosis. One should never take a single negative bronchoscopy too seriously.

DR. ADAMS: Is it not unusual for an empyema necessitatis to burrow in that particular direction?

DR. MALLORY: It is a thing one reads about but does not see very often. I am not absolutely certain about it in this case and admit I am guessing. We found a little scar tissue in the situation which would fit such a hypothesis; but that is not proof.

A PHYSICIAN: Did the second illness have anything to do with the first one?

DR. MALLORY: I doubt if it had the slightest. It is an interesting case from the point of view of determining how long it takes a lung cancer to grow. We have had lung cancers where the story of hemoptysis went back as much as seven years before the onset of any other symptoms at all. Then we occasionally see a case like this where because of some other illness we have had a chest plate within the preceding two years and the early chest plate fails to show lesions. This first plate was taken two years before the final entry and no one has been able to find a trace of tumor though it seems to be a very good plate. We had another case a few days ago where a chest plate was taken four years before and again one year before the symptoms of the final illness. Both of these were negative except for old tuberculous scars but within the last year he developed a sizable tumor mass bigger than a golf ball.

CASE 22362

PRESENTATION OF CASE

First Admission. A fifty-six year old American housewife was admitted complaining of pain and bleeding with defecation.

For about three years the patient had progressive rectal pain with bowel movements, and defecation was often followed by the passage of some bright red blood. For about four months these symptoms were considerably increased in severity. The pain often occurred before, during, and after bowel movements and was sharp and pulsating in character. Occasionally it lasted for an entire day with frequent sharp shooting pains superimposed upon it. In the past she had noted occasional tarry stools but this had not occurred for several months preceding her entry. Currently there was frequent rectal tenesmus often followed only by the passage of a small amount of bright red blood. For about four months she had palpitation, slight dyspnea with exertion, ankle swelling, and puffiness of the eyes in the morning when arising. There was increasing diurnal frequency of micturition and a nocturia of four to five times. On several occasions she noted that urine left standing in the chamber overnight was rather red in appearance. She received medical treatment for hemorrhoids for several months. Her weight decreased from 152 to 114 pounds during the preceding two years and there was concomitant weakness and ready fatigue.

The patient had typhoid fever at the age of eleven years. An appendectomy was performed fourteen years before admission and a Polya gastric resection for duodenal ulcer two years later.

Physical examination showed an emaciated, sick looking middle-aged woman with haggard facies and rather pasty pallor. The mucous membranes were pallid but the tongue was normal in appearance. The lungs were clear and the heart normal. The blood pressure was 105/60. The abdomen was flaccid and the liver extended down to the iliac crest. Its surface was smooth. Inspection of the anus showed two large thrombosed hemorrhoids. Rectal examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine showed a trace of albumin but was otherwise negative. The blood showed a red cell count of 3,600,000, with a hemoglobin of 60 per cent. The white cell count was 9,000, 62 per cent polymorphonuclears, 21 lymphocytes, 1 abnormal lymphocyte, 2 monocytes, and 4 eosinophils. A stool examination was normal and a guaiac test negative. The nonprotein nitrogen of the blood was 26 milligrams.

A flat x-ray film of the abdomen showed normal kidney outlines. There was a soft tissue shadow on the right side which extended down to the crest of the ilium. This had the characteristics of the liver. A barium enema showed no evidence of intrinsic disease of the colon although the transverse colon and hepatic flexure were displaced downward by the enlarged liver.

The patient showed a low-grade fever up to 100.5° during her hospital stay. On the eighth hospital day an anal fissure and hemorrhoids were excised and the patient was discharged on the twelfth postoperative day.

Final Admission, forty-nine days later.

For two weeks following her discharge the patient was much relieved of her previous symptoms although weakness and swelling of the legs prevented her from walking. Six weeks before re-entry she developed severe diarrhea accompanied by cramps across the lower abdomen. The stools were frequent, watery, slimy, and questionably bloody. Two days before coming to the hospital the patient experienced a sharp lancinating pain in her left shoulder and noted that her left hand was swollen. Up to the time of entry swelling of the left hand and forearm increased rapidly and pain in the entire extremity became constant and excruciating in character.

Physical examination showed the left upper extremity to be swollen, shiny, and edematous. Pressure upon the extremity elicited considerable tenderness. Superficial veins over the arm and left side of the chest were dilated. The heart and lungs were negative. The blood pressure was 120/80. The liver extended three fingerbreadths beneath the costal margin and was nodular in consistency. There was slight tenderness in the left lower quadrant and both lower extremities were edematous. Pelvic and rectal examinations were negative.

The temperature was 100.4°, the pulse 100. The respirations were 25.

Two stool examinations showed positive reactions to the guaiac test. The blood showed a red cell count of 3,100,000, with a hemoglobin of 50 per cent. The white cell count was 17,000, 88 per cent polymorphonuclears. A Hinton test was negative. The blood chlorides were 102, the serum protein 4.2 grams and the nonprotein nitrogen 24 milligrams.

A gastrointestinal x-ray series showed a grossly abnormal posterior gastroenterostomy stoma. The distal third of the stomach did not fill with barium. Barium left the stomach rapidly and the motor meal reached the splenic flexure of the colon. There was no evidence of obstruction. The abnormality of the posterior gastroenterostomy stoma was characterized by gross thickening of the mucosa of the stomach and adjacent jejunum. There were two niche-like accumulations of barium, either of which could be ulcerations but neither of which were sufficiently characteristic to be identified as jejunal ulcers. There was an indefinite palpable mass in the region of the stoma. The liver was grossly enlarged and displaced the stomach and colon. There was evidence of fluid in the abdomen. The chest film showed a small quantity of fluid in both costophrenic angles. There was diffusely diminished radiance of both lung fields and the heart shadow was slightly enlarged. The left border was straight and sharp. Another barium enema showed no evidence of gastrocolic fistula or other disease of the colon.

The patient's temperature fluctuated irregularly up to 102° and the swelling and pain in the arm slowly subsided. The patient, however, gradually became weaker and died on the nineteenth hospital day, sixty-eight days after her initial entry.

Notes on the History

Dr. Horace K. Sowles: The type of pain and bleeding described at the start is characteristic of a very low placed intestinal lesion, either inflammatory, or possibly polyp, and is not characteristic of pathology higher up in the bowel.

"In the past she had noted occasional tarry stools . . . ." That is something different from the other symptoms mentioned. It means blood from higher up in the intestinal tract.

"For about four months she had palpitation, slight dyspnea with exertion, ankle swelling, and puffiness of the eyes in the morning when rising." I hesitate to make a comment on a medical problem but that would suggest cardiorenal disease. However, I think there are other things farther on that rule that out. I do not think we need to consider it as a cardiorenal question.

The Polya gastric resection was said to have been done for duodenal ulcer. Lesions of the duodenum are very rarely malignant. It seems rather unlikely that a malignant process would date back that far and that she would still be alive after a pylorectomy for a malignant process. It is possible but not likely. I think it was duodenal ulcer and not malignancy.

The physical examination would tend to rule out cardiorenal disease. The heart was normal, blood pressure low, and later on the nonprotein nitrogen was reported as normal.

They treated the local lesion of which she complained when she came in but that was not enough to account for the very marked loss of weight, the weakness and the fatigue. I think she must have had another lesion higher up in the intestinal tract which was the cause of the more severe systemic disturbances and of the occasional tarry stools. There was another intestinal tract lesion which may have been circulatory. It had a rather sudden onset, but we have no evidence of circulatory disturbance of the bowel. I have seen a case of lymphoma that went on for a year to two years with no general manifestations except bloody stools, with invasion of lymphoid tissues of the intestinal tract but did not invade the other lymphatic tissues or glands for a long period.

"Superficial veins over the arm and left side of the chest were dilated." That is definitely a circulatory disturbance, probably not arterial obstruction, not an embolus, or we would have had an absent pulse and gangrene of the arm. It must be obstruction high up, with whole arm involvement, so that it must be venous disturbance, pressure on the vein, perhaps peripheral thrombosis of the vein.

"The liver extended three fingerbreadths beneath the costal margin and was nodular in consistency." Previously it was reported as smooth, probably the first note was incorrect, although it may have been no fault of the observer. She may now have a thinner abdominal wall and it was easier to feel irregularities of the surface.

There is nothing remarkable in the laboratory findings except that the white count has risen and the percentage of polymorphonuclears is high, denoting an infectious process somewhere.

The blood serum goes with the loss of weight and malnutrition.

X-ray Interpretation

Dr. Aubrey O. Hampton: She had an intravenous pyelogram at the first visit. It was negative. This is the first barium enema. We found nothing wrong. That was at the first admission. This is the second barium enema. Here is the liver. It is quite obvious there and fairly obvious here. If anything, the liver seems to be enlarged. There is a film after evacuation. There is no evidence of gastrocolic fistula at all.

Dr. Sowles: This sudden attack of loose movements and watery diarrhea suggests that she might have perforated a jejunal ulcer through into the colon, but that is not confirmed by the x-ray.

Dr. Hampton: Barium was given by mouth. There is a small quantity in the stomach at this time which emptied out into the jejunum. There is no obstruction to the posterior gastroenterostomy stoma. This looks as if the stomach were amputated just distal to the stoma. There is no stomach to the right of the stoma and the stoma itself shows this irregularity, apparently two ulcerations superimposed. The jejunum itself is below the ulceration. The patient was quite tender and nauseated and compression could not be used. I attempted the second examination after we were sure that she did not have a gastrocolic fistula and at that time I intended to fill the stomach with barium if possible. That was the day before she died, and I was unable to do so.

Differential Diagnosis

Dr. Sowles: The temperature of 102° could be due to an infectious process, as indicated by the high white count and the high polymorphonuclear count, or may possibly be due to metastatic disease in the liver. I feel that she had another and more important lesion than that which brought her to the hospital. The fever, the anal pain and the bright red blood were the prominent symptoms but I do not think they accounted for the loss of weight and the malnutrition. She had a curious circulatory disturbance, a thrombosis of the subclavian vein, possibly circulatory disturbance of the large bowel, which may be thrombosis of veins there causing diarrhea and frequent watery stools. I think she has malignant disease of the stomach, possibly pancreas. I do not think it is a hangover from the duodenal ulcer. She has retroperitoneal extension of this disease to the mediastinum, to the subclavicular region, possibly being a factor in her subclavian thrombosis, probably also extensive retroperitoneal extension downward, which might possibly have interfered with the circulation of the large bowel causing acute intestinal symptoms, a large metastatic involvement of the liver.

Dr. Tracy B. Mallory: Are there any other suggestions?

A Physician: Was she proctoscoped?

Dr. Sowles: No; and that is an important point. She should have been proctoscoped. That is a definite slip-up in diagnostic procedure. Although I do not think we would have found pathology, we should not let her go without proctoscopic examination. She might have had a low polyp not demonstrated by x-ray.

Clinical Diagnosis

Carcinoma of the stomach, metastatic?

Dr. Horace K. Sowles' Diagnosis

Carcinoma of the stomach with metastases.

Anatomic Diagnoses

Carcinoma of the stomach with extension to the jejunum and the pancreas and with metastases to the mesenteric and retroperitoneal lymph nodes, the liver and the adrenals.
Operative scar: Posterior Polya resection of the stomach (for duodenal ulcer).
Peritonitis, chronic fibrous, localized.
Bronchopneumonia, right.
Thrombosis of the splenic vein.
Pulmonary emboli, bilateral, multiple.
Arteriosclerosis, slight aortic and coronary.
Cholecystitis, chronic.

Pathologic Discussion

Dr. Mallory: The autopsy on this patient showed a definite cancer of the stomach. It was situated immediately above and to some extent around the gastrojejunal anastomosis. In spite of the extent of the tumor and its immediate approximation to the anastomosis, we found no obstruction. The tumor had extended directly from the posterior wall of the stomach back into the tissues overlying the pancreas, and large tumor-filled glands were found lying around the pancreas. The pancreas itself, however, was involved to a very slight extent and obviously secondarily. There is no question but that the tumor was primary in the stomach. There were metastases in the liver and in the adrenals.

The surprising feature of the autopsy was a complete thrombosis of the splenic vein. At first we thought it was an actual ingrowth of cancer into the vein but microscopic examination showed that it was only freshly organized thrombus. I should assume, as Dr. Sowles did, that she had a similar thrombosis in the subclavian vein, but we were limited to an abdominal incision and it was impossible to examine it. The immediate cause of death was not suggested from the history. There were multiple pulmonary emboli which very probably arose in the subclavian vein, as we found nothing to account for them in the abdominal cavity.

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SERUM TREATMENT OF ACUTE POLIOMYELITIS

DUE to the unusually low incidence of poliomyelitis in most of the country this summer, the perennial question of the efficacy of convalescent serum treatment has been relatively quiescent. One thing which has come of the recommendation of serum in the preparalytic stage of the disease is the recognition of an increasingly large percentage of nonparalytic cases. While it may be contended that a diagnosis cannot be made with certainty in the absence of paralysis, nevertheless the epidemiologic circumstances, the differentiation from other conditions and the similarity between the symptoms in the nonparalytic type and those in the preparalytic stage of the frank disease leave no doubt as to the nature of the former.

Harmon[1] in reviewing a number of papers in 1934, such as that of Kramer, Aycock, Solomon and Thenebe,[2] where the results in alternate treated and untreated cases were carefully measured, and the report by Park[3] of a large number of treated and untreated cases in New York, came to the conclusion that there was no statistical proof of the value of any type of serum. It was pointed out, however, that the rapid symptomatic response, with drop in temperature and improvement in symptoms following administration of serum, was enough encouragement to warrant continuing its use. Perhaps it should be stated that these preparalytic symptoms in themselves do not appear to be sufficiently severe to justify drastic measures of relief. Furthermore, since there seems to be no correlation between severity of the early symptoms and paralysis, it does not follow that mitigation of symptoms would have any effect on paralysis. Moreover, the problem of measuring the comparative outcome of treated and untreated cases presents many difficulties, for the reason that the extent of involvement cannot be foretold from any of the symptoms in the preparalytic stage. Even after paralysis has appeared, the amount of spontaneous recovery is likewise unpredictable, and the time element here involved introduces a further obstacle. With these considerations in mind, the tendency to at least a degree of spontaneous recovery offers a great chance to the physician who has administered the serum with hope.

From a review of the now considerable literature on the subject, it would appear that the most definite, hopeful thing which has come out of convalescent serum treatment of poliomyelitis is the fact that a diagnosis of poliomyelitis in the preparalytic stage is no longer taken as meaning inevitable paralysis. With increasing attention to the early stage of the disease, an ever-increasing proportion of nonparalytic cases is being uncovered, now well over 50 per cent.

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THE CERTIFICATION OF SPECIALISTS

FOR more than fifty years the medical profession has been trying to interest the laity in the important safeguards to well-being through efficient public health agencies and the service of well-trained physicians. Although some nonprofessional and public-spirited citizens have united with doctors in efforts to secure legislation which would raise the standards of medical practice, a proportion of the general public has been inclined to view with suspicion the recommendations of the profession to the several legislatures for laws which were designed to assure the people of competent practitioners of the healing art. The result is that even the best of the laws governing the licensing of physicians to engage in practice at the present time assure only average ability of the majority of

the doctors of this country. There seems to pervade the minds of our law-makers in some instances a purpose to protect the doctor more than the health of the people.

It is an established fact that the science of medicine has progressed more rapidly than its utilization by the average practitioner and that many people are unable to discriminate when obliged to select a medical attendant, and since there is only average ability in a part of the profession, there must be a proportion of lower grade practitioners. This situation imposes a risk on uninformed persons who may suffer through the unwise selection of a physician. Since the possibility of this predicament is recognized, movements by organized medicine have been underway for several years to certify to the qualifications of well-trained men in different departments of medical practice. The American College of Surgeons developed this plan for the certification of competent surgeons several years ago and this example has been followed by twelve other organized societies of national scope which are now prepared to certify to the proficiency of doctors in specified fields of practice.

The latest movement in this direction is that arranged by the American Board of Internal Medicine and full explanation of the composition and purpose of this organization will be found on page 470 of this issue.

This and other plans to assure to the public the best possible care in any designated field of practice should be encouraged. With the growth of specialties there will be an increase of apprehension on the part of the public that the general practitioner will be driven from his long-time honorable position.

This is unlikely but there will certainly develop changed conditions and relations of concern to the public and the profession. In the first place, certified specialists will be the resource of the general practitioner whenever he is confronted with uncertainties of diagnosis or treatment. On the other hand, there will have to be an adjustment of the relation of the specialist and the family attendant.

The situation at the present time is not always fair to the general man and the several groups of specialists must be willing to deal justly with those who seek their aid. Details of ethical practice must be observed between general practitioners and specialists in so far as this applies to recognized principles.

In these earlier years of plans for the certification of specialists, there will be some unavoidable difficulties, but these will disappear when better preparation for practice shall have become general. That is, there must be on the average a better type of general practitioner who is worthy of the respect of his specialist associate.

The future dignity of the profession in all of its branches will be assured when no one, other than well-educated doctors, is given the right to practice.

The prospective doctor must realize that the medical education of a given period should not be regarded as adequate for later years and that if he expects to hold an honorable position in his calling his education must be a continuous process.

It may be that the public will some time demand that there must be evidence of progress among civilian physicians as is required in the professional service of the Army and Navy.

The public is growing more intelligent about the resources of medicine. It may demand assurance of the standing of practitioners. The plans for the certification of specialists will, we believe, tend to promote better general medical practice.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

BOCK, ARLIE V. A.B., Ph.D., M.D. Harvard University Medical School 1915. Henry K. Oliver Professor of Hygiene, Harvard University. Physician, Massachusetts General Hospital. His subject is The Use and Abuse of Blood Transfusions. Page 421. Address: 15 Holyoke Street, Cambridge, Mass.

HAMILTON, ALICE. M.A., M.D. University of Michigan Medical School 1893. Assistant Professor of Industrial Medicine, Harvard University Medical School 1919-1935. Member, Health Organization of League of Nations 1924-1930. Consultant, United States Public Health Service and United States Department of Labor 1936-. Her subject is Some New and Unfamiliar Industrial Poisons. Page 425. Address: Hadlyme Ferry, Hadlyme, Conn.

JONES, CHESTER M. A.B., M.D. Harvard University Medical School 1919. Assistant Professor in Medicine, Harvard University Medical School. His subject is Newer Concepts of Liver Disease. Page 432. Address: Massachusetts General Hospital, Boston, Mass.

JOHNSON, ALLEN S. A.B., B.A., D.N.B., M.D. Harvard University Medical School 1927. F.A.C.P. Assistant Visiting Physician, Springfield Hospital. Visiting Physician, Health Department Hospital, Springfield. His subject is Sodium Chloride Therapy. Page 438. Address: 121 Chestnut Street, Springfield, Mass.

SPROULL, JOHN. M.D. Boston University School of Medicine 1901. His subject is A General Practitioner's Views on the Treatment of Angina Pectoris. Page 443. Address: 50 Merrimack Street, Haverhill, Mass.

WHITE, JAMES C. A.B., M.D. Harvard University Medical School 1923. F.A.C.S. Assistant Visiting Surgeon, Massachusetts General Hospital. Assistant Professor and Tutor in Surgery, Harvard University Medical School. His subject is Progress in the Surgery of the Autonomic Nervous System in 1935. Page 453. Address: Massachusetts General Hospital, Boston, Mass.

MISCELLANY

THE AMERICAN BOARD OF INTERNAL MEDICINE (INC.)

The American Board of Internal Medicine, incorporated February 28, 1936, completed its organization on June 15, 1936. The officers chosen were Walter L. Bierring, M.D., Des Moines, Chairman; Jonathan C. Meakins, M.D., Montreal, Vice-Chairman, and O. H. Perry Pepper, M.D., Philadelphia, Secretary-Treasurer. These officers with the following six members constitute the present membership of the board: David P. Barr, M.D., St. Louis; Reginald Fitz, M.D., Boston; Ernest E. Irons, M.D., Chicago; William S. Middleton, M.D., Madison; John H. Musser, M.D., New Orleans, and G. Gill Richards, M.D., Salt Lake City.

The term of office of each member will be three years, and no member can serve more than two consecutive three-year terms.

The organization of the Board is the result of effective effort on the part of the American College of Physicians in conjunction with the Section on Practice of Medicine of the American Medical Association and these two organizations are represented in the membership of the Board on a five to four ratio, respectively.

The American Board of Internal Medicine had previously received the official approval of the two bodies fostering its organization, as well as that of the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

The purpose of the Board will be the certification of specialists in the field of internal medicine, and the establishment of qualifications with the required examination procedure for such certification.

While the Board is at present chiefly concerned with the qualification and procedure for certification in the general field of internal medicine, it is intended to inaugurate immediately after July 1, 1937, similar qualification and procedure for additional certification in certain of the more restricted and specialized branches of internal medicine, as gastroenterology, cardiology, metabolic diseases, tuberculosis, allergic diseases, et cetera. Such special certification will be considered only for candidates who have passed at least the written examination required for certification in general internal medicine. The operation of such a plan will require the active participation and co-operation of recognized representatives from each of such special fields of medicine.

Each applicant for admission to the examination in internal medicine will be required to meet the following standards:

GENERAL QUALIFICATIONS

1. Satisfactory moral and ethical standing in the profession.
2. Membership in the American Medical Association or, by courtesy, membership in such Canadian or other medical societies as are recognized for this purpose by the Council on Medical Education and Hospitals of the American Medical Association. Except as here provided, membership in other societies will not be required.

PROFESSIONAL STANDING

1. Graduation from a medical school of the United States or Canada recognized by the Council on Medical Education and Hospitals of the American Medical Association.
2. Completion of an internship of not less than one year in a hospital approved by the same council.
3. In the case of an applicant whose training has been received outside of the United States and Canada, his credentials must be satisfactory to the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

SPECIAL TRAINING

1. Five years must elapse after completion of a year's internship in a hospital approved for interne training before the candidate is eligible for examination.
2. Three years of this period must be devoted to special training in internal medicine. This requirement should include a period of at least several months of graduate work under proper supervision in anatomy, physiology, biochemistry, pathology, bacteriology, or pharmacology, particularly as related to the practice of internal medicine.

   This work may be carried on in any domestic or foreign medical school or laboratory recognized by the Council on Medical Education and Hospitals of the American Medical Association as offering appropriate facilities for this type of postgraduate experience; or it may include a period of at least several months of graduate work under proper supervision in internal medicine or in its restricted and specialized branches in any domestic or foreign hospital, clinic, or dispensary, recognized by the above Council as offering appropriate facilities for this type of postgraduate experience.
3. A period of not less than two years of special practice in the field of internal medicine or in its more restricted and specialized branches.

The American Board of Internal Medicine does

not propose to establish fixed rules for the preliminary training of candidates for certification in this field. Broad general principles for training, however, may be outlined, although such suggestions as are made must, of necessity, be subject to constant changes reflecting the dynamic nature of the specialty.

A sound knowledge of physiology, biochemistry, pharmacology, anatomy, bacteriology, and pathology, in so far as they apply to disease, is regarded as essential for continued progress of the individual who practices internal medicine. The more factual knowledge of medicine and its basic sciences is not sufficient. The candidate must have had training in their use in furthering his understanding of clinical medicine. This implies practical experience under the guidance of older men who bring to their clinical problems ripe knowledge and critical judgment. Preparation to meet this requirement adequately may be even more difficult to obtain than the so-called scientific training. It may, however, be acquired in the following ways:

(a) By work in a well-organized hospital outdoor clinic conducted by competent physicians.

(b) By a prolonged period of resident hospital appointments likewise directed by skilled physicians.

(c) By a period of training in intimate association with a well-trained and critical physician who has taken the trouble to teach and guide his assistant rather than to require him only to carry out the minor drudgery of a busy practice.

4. The Board does not consider it to the best interests of internal medicine in this country that rigid rules as to where or how the training outlined above is to be obtained. Medical teaching and knowledge are international. The opportunities of all prospective candidates are not the same. Some may have the opportunity of widening their knowledge by a period of study abroad. Others, at the other extreme, may be restricted to a comparatively narrow geographic area and their detailed training must be obtained in short periods scattered over a long time. Although it is laid down that at least five years must elapse between the termination of the first interne year and the time when the candidate is eligible to take the examination, a longer period is advisable. The Board wishes to emphasize that the time and training are but means to the end of acquiring a broadness and depth of knowledge of internal medicine which the candidate must demonstrate to the Board in order to justify it in certifying that he is competent to practice internal medicine as a specialty. The responsibility of acquiring the knowledge as best he may rests with the candidate, while the responsibility of maintaining the standard of knowledge required for certification devolves on the Board.

METHOD OF EXAMINATION

The examination required of candidates for certification as specialists in Internal Medicine will comprise, Part I (written) and Part II (practical or clinical).

Part I The written examination is to be held simultaneously in different sections of the United States and Canada and will include:

(a) Questions in applied physiology, physiological chemistry, pathology, pharmacology, and the cultural aspects of medicine.

(b) Questions in general internal medicine.

The first written examination will be held in December, 1936, and candidates successful in this written test will be eligible for the first practical or clinical examination which will be conducted by members of the Board near the time for the annual session of the American College of Physicians at St. Louis in April, 1937. The second practical examination will be held at Philadelphia near the time of the annual session of the American Medical Association in Atlantic City in June, 1937.

The fee for examination is forty dollars which must accompany the application and an additional fee of ten dollars is required when the certificate is issued.

Application blanks and further information can be obtained by addressing the office of the chairman, Walter L. Bierring, M.D., 406 Sixth Avenue, Des Moines, Iowa, U. S. A.

THE CHAIRMAN OF THE MASSACHUSETTS BOARD OF REGISTRATION IN MEDICINE

Dr. Francis R. Mahony of Lowell was elected Chairman of the Massachusetts Board of Registration in Medicine at a meeting of the Board August 28, 1936, to fill the position made vacant by the resignation of Dr. Charles P. Sylvester.

Dr. Sylvester's resignation was because of the necessity of adopting measures which will bring about restoration of his health. His service on the board has been recognized as highly meritorious and his reputation as a conscientious public servant is established.

EXCESS OF DEATHS OVER BIRTHS IN FRANCE

Deaths exceeded births in France during 1935, according to *La Science et la Vie*. Births during the year numbered 638,881, and there were 658,357 deaths—a morbidity excess of nearly 20,000. During 1934 births exceeded deaths by about 43,000. Unemployment and rising cost of living in France are blamed for the situation. At the same time Germany showed an excess of 480,000 births over deaths during 1935.—*Science Service.*

OFFICERS OF THE NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

The re-election of Mr. William Fellowes Morgan as President of the National Society for the Prevention of Blindness has been announced by Lewis H. Carris, Managing Director. Other officers elected are Dr. Francis Park Lewis of Buffalo, N. Y., First Vice-President; Mr. Russell Tyson of Chicago, Ill., Second Vice-President, and Mr. Preston S. Millar of New York City, Third Vice-President.

Mr. Carris announced, also, that Dr. Edward C. Ellett of Memphis, Tenn., had been elected a member of the Society's Board of Directors, to succeed the late Dr. William H. Wilmer, of Baltimore, Md. Dr. Ellett is a graduate of the University of Pennsylvania and has been a member of the American Ophthalmological Society since 1912.

The annual conference of the Society will be held in Columbus, Ohio, December 3 to 5.

CORRESPONDENCE

INDUSTRIAL CONDITIONS IN ENGLAND IN 1842—THE GRINDERS AND THE POTTERY WORKERS

Editor, *New England Journal of Medicine,*

The following quotation is from the chapter "March Past" in Edith Sitwell's book "Victoria of England" (Faber and Faber, Ltd., London, 1936). The author pictures the different types of industrial workers marching past a given point.

"What is this terrible sound, as of multitudinous wooden shuttles, or air being driven through thousands of wooden tubes? What is this cloud of black dust, expectorated from dying lungs? It is the sound and symptom of the industrial disease from which the Grinders die.

"'In Sheffield,' wrote Dr. Knight of that city, 'there are some two thousand five hundred grinders at work. About one hundred and fifty (eighty men and seventy boys) are fork grinders; these die between the twenty-eighth and thirty-second year. The razor grinders, who grind wet as well as dry, die between forty and forty-five years; and the table cutlery grinders, who grind wet, die between the forty-fifth and fiftieth year.' This comes from the sharp-edged metal dust particles freed in the cutting, which fill the air and are thus inhaled,' and, too, from the bent position in which they must work, and in which the chest and stomach are cramped. Here they come, with their yellow faces, their 'features expressing anxiety,' their rough hoarse voices, and that loud cough, 'whose sound is as if air were driven through a wooden tube.' Dr. Knight adds that he has often told grinders with the first symptoms of this disease that if they returned to work they would die. It was useless, for 'he who is once a grinder falls into despair, as if he had sold his soul to the devil.'

"What is this feeble sound, this hopeless whispering of multitudes, so faint it seems the despairing prayer of those about to die? It is the voice of the Pottery Workers in the grip too of their industrial disease. Here they come, twitching and writhing as if they were being agitated by some vast machine, some Moloch which folds them in its grasp. Their work is to dip the finished pottery into fluid containing great quantities of lead or arsenic. The hands, the clothing of these men, women, and children, are perpetually wet with this fluid, the skin softens and is scraped away by the contact with hard or rough objects, and their fate has them in its grasp, for into these wounds, these soft places, the lead, the arsenic is absorbed. Violent pain, serious disease of the stomach and intestines, tuberculosis, but most often epilepsy, are the results. Amongst men, partial paralysis of the hand muscles, or paralysis of whole limbs, is frequent. . . . In one factory, according to the same commission, four men, all epileptic and affected with severe colic, and eleven boys, several of them epileptic, were found in the dippinghouse. In those rooms of the potteries in which the stonework is scoured, the air is filled with the dust of ground flint which has the same result as the steel dust on the Sheffield grinders. Breathlessness, inability to lie down, sore throat, and a terrible cough—these are the result . . . . Until at last they come to have so feeble a voice they can scarcely be heard. They, too, all die of tuberculosis."

Very truly yours,

WM. PEARCE COUES, M.D.

Prout's Neck, Maine,
August 25, 1936.

AN UNUSUAL SERIES OF TAPPINGS

August 10, 1936.

Editor, *New England Journal of Medicine,*

I beg to report the following case: Mrs. W., aged 75, weight 104 lbs., afflicted with hypertrophic cirrhosis of liver, valvular disease of heart, and arteriosclerosis. The first abdominal tapping was done August 15, 1930. The seventy-second tap was on July 12, 1936. Amount of fluid removed during these years was 144¼ gallons, weighing 1268 lbs. She now requires tapping at about three-week intervals, the average amount of fluid removed being 11½ qts. and weighing 24 to 25 lbs.

Mrs. W. suffers no pain, and is not confined to bed. She does her own housework and thinks nothing of a hundred-mile ride in an automobile.

Very truly yours,

ALBERT C. LEACH, M.D.

Orange, Massachusetts.

RECENT DEATHS

BOYDEN—ARTHUR HENRY BOYDEN, M.D., of 4 Nottingham Road, whose office was at 390 Main Street, Worcester, Massachusetts, died at his home, August 23, 1936, after a long illness. Dr. Boyden was born in Worcester, September 29, 1879, the son of Charles O. Boyden and Sarah J. (Kennington) Boyden.

After acquiring his early education in the schools

of his native city and the Boston High School, he entered Tufts College and received his A.B. degree therefrom. He then entered Tufts College Medical School, graduated in 1909, and served his internship in the Worcester City Hospital. He later became a member of the Surgical Staff.

Dr. Boyden was a Fellow of the Massachusetts Medical Society and the American Medical Association. He was also a member of the American College of Surgeons, Quinsigamond Lodge, A. F. & A. M., and the Worcester Economic Club.

Dr. Boyden is survived by his widow, Mrs. C. I. (Bottomly) Boyden; a daughter, Miss Elizabeth Boyden of Worcester, and two sisters, Mrs. Lillian Seymour, of Andover, and Miss Florence D. Boyden, of Boston.

BURACK—ABRAHAM BURACK, M.D., of 95 Waldo Street, Brockton, Massachusetts, whose office was at 142 Main Street, died at the Beth Israel Hospital, Boston, August 23, 1936, after a long illness.

Dr. Burack was born in Boston in 1889 and graduated from the Tufts College Medical School in 1912. He was a Fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, Mrs. Sarah Burack, and a son, Jason Burack, survive him.

SMITH—FRANK HERBERT SMITH, M.D., of Hadley, Massachusetts, died at his home, August 23, 1936. Dr. Smith was born in North Hadley in 1871 and was educated at Hopkins Academy, Amherst College, and the University of Pennsylvania School of Medicine where his medical degree was conferred in 1898.

After practicing in Philadelphia for two years, Dr. Smith returned to Hadley and established a large practice. He became physician to Amherst College in 1929. His health failed nearly a year ago and he retired from active work.

Dr. Smith was a Fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, Mrs. Grace Howe Smith; a son, Myron Smith, an electrical engineer of Boston; and a daughter, Eleanor Smith, professor of bacteriology at Smith College, survive him.

NOTICES

TERCENTENARY SESSION OF THE HARVARD MEDICAL SCHOOL

SEPTEMBER 14 AND 15, 1936

As part of the University celebration, the Medical School and the Medical Alumni Association invite the graduates of the School to return on September 14 and 15 for the Medical School Exercises and Medical Alumni Reunion. These will immediately precede the final Cambridge exercises on September 16, 17 and 18.

The Medical School Exercises will include:

Demonstrations, special clinics, discussions and exhibits at the various hospitals associated with the Harvard Medical School.

Four carefully planned symposia programs, presented by the Harvard Medical Faculty, on

Nutrition and the Deficiency Diseases
Chairman, Dr. George R. Minot

The Nervous System; Central and Sympathetic
Chairman, Dr. Walter B. Cannon

The Infectious Diseases
Chairman, Dr. Hans Zinsser

The Endocrine Glands
Chairman, Dr. J. Howard Means

The business meeting and the dinner of the Harvard Medical Alumni Association will be held on the evening of September 15 at the Harvard Club, at 6:30 and 7 p. m. respectively. This meeting has been postponed from its usual time in June in honor of the Tercentenary and to encourage the return at this time of as many graduates as possible.

PROGRAM OF THE TERCENTENARY SESSION OF THE MEDICAL SCHOOL

MONDAY, SEPTEMBER 14

9:00 a. m.-12:30 p. m. Clinics and demonstrations

The "open house" demonstrations and exhibits of the summer will be continued during this morning. The members of the staffs will be present to discuss their work informally, and many of the departments and hospitals will offer special clinics and demonstrations. The full program will be announced at a later date in the Medical Alumni Bulletin.

12:30 p. m. Buffet luncheon in Vanderbilt Hall

2:00-5:00 p. m. Harvard Medical School, Building D:

Introduction to the Symposia
Dr. David L. Edsall, Dean Emeritus

Nutrition and the Deficiency Diseases

Chairman: Dr. George R. Minot

Dr. J. L. Gamble—Extracellular Fluid and Its Maintenance
Dr. C. M. Jones—Protein Deficiency
Dr. C. W. Heath — Mechanism of Hemoglobin Deficiency
Dr. W. B. Castle — The Relationship of Defective Nutrition to Changes in the Gastro-Intestinal Tract
Dr. S. B. Wolbach—Vitamin C and the Formation of Intercellular Material
Dr. K. D. Blackfan—Progress in the Early Recognition of Vitamin Deficiency States
Dr. P. Howe—Oral Pathology in Relation to Avitaminosis
Dr. M. B. Strauss — Nerve Disorders Arising from Defective Nutrition
Dr. E. P. Joslin—Protamine Insulin and Its Advantages

5:00 p. m. Tea in the Medical School Quadrangle

Monday evening is held open for possible Medical class reunions and hospital reunions.

TUESDAY, SEPTEMBER 15

Instead of two morning sessions and one afternoon session as originally announced, there will be three simultaneous programs, each extending from 10:00 a. m. to 12:00 m. and from 2:00 to 4:00 p. m., at the Harvard Medical School.

The Nervous System; Central and Sympathetic

Chairman: Dr. Walter B. Cannon

Dr. J. C. White—Surgery of the Sympathetic Nervous System
Dr. A. Rosenblueth — Chemical Mediation of Nervous Effects
Drs. J. B. Ayer and H. R. Viets—The Use of Prostigmine in Myasthenia Gravis
Dr. H. Davis—The Electrical Activity of the Human Brain
Drs. F. A. Gibbs and W. G. Lennox—The Electrical Activity of the Brain in Epilepsy
Dr. S. Cobb—Cerebral Circulation
Dr. S. Weiss—Syncope and Collapse
Dr. T. J. Putnam — The Pathogenesis of Multiple Sclerosis

The Infectious Diseases

Chairman: Dr. Hans Zinsser

Dr. Hans Zinsser—Recent Advances in the Study of Typhus Fever
Dr. C. F. McKhann — The Immunological Application of Placental Extract
Dr. W. G. Smillie—Epidemiological Studies on the Virus of Influenza
Drs. C. S. Keefer and W. W. Spink—Immune Reactions in Gonococcal Infections
Dr. A. W. Sellards—Yellow Fever
Dr. C. Lyons—Antibacterial Immunity in Hemolytic Streptococcic Infections
Dr. E. S. A. Robinson—The Antiserum Treatment of Pneumonia from the Standpoint of Public Health
Dr. M. Finland—Some Aspects of Pneumococcus Infection in Man
Dr. R. P. Strong—Studies on Filarioidea
Dr. D. L. Augustine — Trichinosis; Incidence and Diagnostic Tests
Drs. H. Pinkerton and G. M. Hass — Cultivation of Rickettsia in Tissue Culture

The Endocrine Glands

Chairman: Dr. J. Howard Means

Dr. G. B. Wislocki — The Blood Supply to the Hypophysis
Dr. H. B. Friedgood — The Nervous Control of the Anterior Hypophysis
Dr. E. C. Cutler—Diabetes Insipidus: Its Relation to Hypophysis and Thyroid
Dr. J. C. Aub — Hypophyseal-Parathyroid Relationships
Dr. A. B. Hastings—Factors Governing the Calcium Equilibria of the Body
Dr. F. Albright — The Action of the Parathyroid Hormone upon the Skeleton
Dr. E. D. Churchill — The Surgery of the Parathyroids
Dr. W. T. Salter—The Genesis of Thyroid Protein
12:30 p. m. Buffet Luncheon in Vanderbilt Hall.
6:30 p. m. Business Meeting of the Medical Alumni Association at the Harvard Club.
7:00 p. m. Dinner of the Alumni Association at the Harvard Club.

REMOVALS

ALEXANDER A. LEVI, M.D., announces the removal of his office from 485 Commonwealth Avenue to 481 Beacon Street, Boston. Telephone: Kenmore 8000.

SELWYN L. STEEL, M.D., announces the removal of his office from 128 Chestnut Street to 320 Beacon Street, Boston. Telephone: Kenmore 8100.

HORACE BINNEY, M.D., announces the removal of his office to 370 Commonwealth Avenue, Boston. Telephone: Kenmore 0306.

SAMUEL L. GARGILL, M.D., announces the removal of his office to 481 Beacon Street, Boston. Telephone: Kenmore 8000.

NOTICE OF MEETING

PENTUCKET ASSOCIATION OF PHYSICIANS
1936-37

The place of meeting for September 10 and June 24 is "Duck In." Tel. Merrimac 280. All other meetings at Hotel Bartlett, 95 Main Street, Haverhill. Tel. Haverhill 3680. Hour of meeting 8:30 p. m. Dinner followed by address.

September 10—Dr. Donald Munro
Assistant Professor of Neuro-Surgery, Harvard; Visiting Surgeon for Neuro-Surgery, Boston City Hospital.
Subject: "The Responsibility of the General Practitioner in Relation to Common Neuro-Surgical Conditions."

October 8—Dr. Arthur W. Allen
Chairman, Surgical Staff, Massachusetts General Hospital; Vice-President, American College of Surgeons.
Subject: "Diseases of the Peripheral Vascular System."

November 12—Dr. W. Richard Ohler
Internist, Boston City Hospital.
Subject: "The Clinical Interpretation of Laboratory Procedures."

December 10—Dr. Horace K. Sowles
Surgical Staff, Massachusetts General Hospital; Surgeon, Faulkner Hospital.
Subject: "Carcinoma of the Intestines."

January 14—Dr. Samuel A. Levine
Cardiologist, Peter Bent Brigham and Beth Israel Hospitals.
Subject: "Some Interesting Experiences of a Heart Specialist."

February 11—Dr. Clarence A. Bonner
Superintendent, Danvers State Hospital.
Subject: "Some of the Preventive Aspects of the Mental Health Problem."

March 11—Dr. Howard M. Clute
Surgical Chief, Massachusetts Memorial and Carney Hospitals; Professor of Surgery, Tufts College Medical School.
Subject: "Problems of the Upper Abdomen."

April 8—Dr. Frank A. Pemberton
Surgical Chief, Free Hospital for Women.
Subject: "Progress in Gynecology."

May 13—Dr. W. Russell MacAusland
Assistant Professor of Orthopedics, Tufts College Medical School; Trustee Canton School for Crippled Children.
Subject: "Some of the Recent Advances in Fracture Treatment."

June 24—Dr. Morris Fishbein
Editor of the *Journal of the American Medical Association*, Chicago, Illinois.
Subject: "The Outlook for the Profession."

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, SEPTEMBER 7, 1936

Saturday, September 12—

*10 a. m. - 12 m. Staff Rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

September 7, 8, and 9—The Cancer Institute. See page 309, issue of August 13.

September 7-10—International Union against Tuberculosis. See page 554, issue of March 12.

September 7-11—American Congress of Physical Therapy will meet at the Waldorf-Astoria, New York City. See page 52, issue of July 2.

September 9 to 12—Sixth Congress of the International Society for Urology. For details address Dr. Theodor Hryntschak, Rathausstrasse 3, Wien, I.

September 10-June 24—Pentucket Association of Physicians. See page 474.

September 14 and 15—Tercentenary Session of the Harvard Medical School. See page 1166, issue of June 4, and page 473 of this issue.

September 16-21—First International Congress of Sanatoria and Private Nursing Homes. See page 803, issue of April 16, and page 264, issue of August 6.

September 22, 23, 24—Twelfth Clinical Congress of the Connecticut State Medical Society. See page 217, issue of July 30.

October 12-18—Third International Congress on Malaria. See page 1076, issue of May 21.

October 19-23—Clinical Congress of the American College of Surgeons. See page 180, issue of January 23.

October 19-31—1936 Graduate Fortnight of the New York Academy of Medicine. See page 1221, issue of June 11.

October 20-22—Academy of Physical Medicine, Annual Meeting, Hotel Statler, Boston.

October 20-23—The American Public Health Association. See page 1226, issue of June 11.

December 3-5—Annual Conference of the National Society for the Prevention of Blindness, Columbus, Ohio.

March 30 - April 2, 1937—First International Conference on Fever Therapy. Postponement notice. See page 52, issue of July 2.

April 21-24, 1937—American Society for Experimental Pathology. See page 1075, issue of May 21.

DISTRICT MEDICAL SOCIETIES

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

October 7—Bear Hill Golf Club, Stoneham.
November 18—Bear Hill Golf Club, Stoneham.
January 13, 1937—Bear Hill Golf Club, Stoneham.
March 16, 1937—Danvers State Hospital, Danvers.
May 11, 1937—Bear Hill Golf Club, Stoneham.

KENNETH L. MACLACHLAN, M.D., Secretary.
1 Bellevue Avenue, Melrose.

PLYMOUTH DISTRICT MEDICAL SOCIETY

October 15—11 a. m. at the Moore Hospital, Brockton.

FRED F. WEINER, M.D., Secretary.
231 Main Street, Brockton.

WORCESTER DISTRICT MEDICAL SOCIETY

September 23—At the Milford Hospital, Milford, Mass. 4:30 p. m.: Visitation of the Milford Hospital unit, which has been recently refinished and added to. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Scientific program and business session. The speakers for this meeting will be Dr. Richard Miller and Dr. Cadis Phipps of Boston, who will give a symposium on Peptic Ulcer, with Dr. Miller discussing the surgical aspects and Dr. Phipps the medical aspects of this condition.

October 14—Rutland State Sanatorium, Rutland, Mass. 6:15 p. m.: Dinner—complimentary by the State Hospital. 7:30 p. m.: Business session and scientific program. Speakers and subjects to be announced in a later issue of the Journal.

November 5—At 4:30, in the rooms of the Worcester Medical Library, Inc., at 34 Elm Street, Worcester, will be held the fall Censors' meeting.

November 11—Grafton State Hospital, North Grafton, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

December 9—St. Vincent Hospital, Worcester, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

January 13, 1937—Worcester City Hospital, Worcester, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

February 10, 1937—Worcester State Hospital, Worcester, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

March 10, 1937—The Memorial Hospital, Worcester, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

April 14, 1937—Worcester Hahnemann Hospital, Worcester, Mass. 6:15 p. m.: Dinner—complimentary by the hospital. 7:30 p. m.: Business session and scientific program.

May 6, 1937—At 4:30 in the rooms of the Worcester Medical Library, Inc., at 34 Elm Street, Worcester, will be held the spring meeting of the Board of Censors.

Wednesday Afternoon and Evening, May 12, 1937—Annual Meeting. Time and place for this meeting will be announced in an early spring issue of the Journal.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester.

BOOKS RECEIVED FOR REVIEW

Studies from The Rockefeller Institute for Medical Research. Reprints. Volume 98. 597 pp. New York: The Rockefeller Institute for Medical Research. 1936.

The Therapeutic Agents of the Pyrrole and Pyridine Group. Including the Tropinol, Scopoline, Ecgonine, and Granatoline Derivatives. The Relation between Their Chemical Constitution and Pharmacologic Action. W. F. von Oettingen. 258 pp. Ann Arbor: Edwards Brothers. Inc. $4.75.

Pathological Physiology and Clinical Description of the Anemias. William Bosworth Castle, and George Richards Minot. Edited by Henry A. Christian. 205 pp. New York: Oxford University Press. $3.00.

Interpretation of Laboratory Findings. Raymond H. Goodale. 170 pp. Philadelphia: F. A. Davis Company.

Amino Acid and Ammonia Metabolism in Liver Diseases. Esben Kirk. 147 pp. Copenhagen: Levin & Munksgaard, Publishers.

Heart Disease and Tuberculosis. Efforts Includ-

ing Methods of Diaphragmatic and Costal Respiration to Lessen Their Prevalence. S. Adolphus Knopf. 108 pp. New York: The Livingston Press. $1.25.

Orthopaedic Surgery. Walter Mercer. Second Edition. 906 pp. Baltimore: William Wood & Company. $10.00.

The Toxaemias of Pregnancy. Dame Louise McIlroy. 355 pp. Baltimore: William Wood & Company. $5.00.

The Operations of Surgery. R. P. Rowlands and Philip Turner. Eighth Edition, Volume I. 1045 pp. Baltimore: William Wood & Company. $10.00.

Report of the Penrose Research Laboratory Formerly Laboratory and Museum of Comparative Pathology of the Zoological Society of Philadelphia. Herbert Fox. 30 pp. 1936.

The Oxford Medicine. By Various Authors. Edited by Henry A. Christian. 634 pp. New York: Oxford University Press. $10.00.

Vascular Disorders of the Limbs. Described for Practitioners and Students. Sir Thomas Lewis. 111 pp. New York: The Macmillan Company. $2.00.

Endocrinology in Modern Practice. William Wolf. 1018 pp. Philadelphia and London: W. B. Saunders Company. $10.00.

A Text-Book of Physiology. H. E. Roaf. Second Edition. 679 pp. Baltimore: William Wood & Company. $6.75.

Pathology of the Nervous System. J. Henry Biggart. 335 pp. Baltimore: William Wood & Company. $5.25.

A Preface to Nervous Disease. Stanley Cobb. 173 pp. Baltimore: William Wood & Company. $2.50.

BOOK REVIEWS

Synopsis of Diseases of the Heart and Arteries. George R. Herrmann. 344 pp. St. Louis: The C. V. Mosby Company. $4.00.

This volume is unique among American publications in the field of cardiology. Although its title indicates that it is a "Synopsis" and the author describes it as an "indexed epitome of the principles and modern conception of cardiologic practice", it is amazing how much useful material is contained in such a small and readable handbook. All the common cardiovascular conditions are adequately discussed. This even includes chapters on electrocardiography and cardiologic roentgenology and peripheral vascular disease. The various instruments and methods of study are taken up, such as the oscillometer and the determination of the venous pressure. The numerous illustrations and figures are extremely well chosen and add a great deal to clarify both the pathologic and the physiologic aspect of the subject.

Students and practitioners, for whom this book is primarily intended, will be amply rewarded for the time spent in reading the various chapters and may even use it for reference purposes when puzzled by the application of certain specific procedures of cardiovascular study or therapy.

Security Against Sickness: A Study of Health Insurance. I. S. Falk. 423 pp. New York: Doubleday, Doran & Company, Inc. $4.00.

The author of this book is well qualified from long study of the subject to discuss health insurance. The factual data on the organization of medical practice are well presented but do not give any new information although some of the figures are brought up to date. There is an excellent summary of health insurance in the leading countries of Europe. These factual data cannot be questioned as to their accuracy.

The last section of the book is entitled "Basic Principles for an American Program," and this is by all means the most interesting portion of the book as it consists largely of a critical discussion of the possible principles for health insurance in this country. The book concludes with a statement of nineteen basic principles which should be considered in developing an insurance plan for the United States. The author emphasizes repeatedly that "health insurance is not a system of medical practice. It is a system of paying costs of sickness through budget and pre-payment."

The author frankly assumes that health insurance will be adopted in this country eventually. One may not agree with this point of view, but the book is well worth careful reading even by those who do not accept the author's conclusion.

The Operations of Surgery. R. P. Rowlands and Philip Turner. Eighth Edition, Volume 1. 1045 pp. Baltimore: William Wood & Company. $10.00.

This book is intended as an aid to candidates for higher degrees of surgery in England, and as a reference book for those who practice surgery. The former purpose makes for misplaced emphasis, and infrequently practiced operative procedures are given a considerable space because of their purely academic importance. Thus 13 pages are devoted to "Excision of the Elbow" and only five to "Infections of the Hand."

The authors have rewritten the previous edition of this work and endeavored to incorporate recent advances, but on a number of points the literature could not have been consulted widely. Cushing's statistics on operative mortality for patients with brain tumors are those of 1915 rather than those of late publication. The most recently quoted paper on pericardiolysis is one in 1915 despite the fact that Paul White reviewed his and Churchill's series in the *Lancet* only last year.

American surgeons will take exception to many of the teachings in this book. The statement that "In early cases of true primary toxic goiter, operation is not indicated" will find few proponents among goiter surgeons in this country.

The first volume of the present edition deals with

the upper extremity, head and neck, thorax, lower extremity and vertebral column. As a review of standardized surgical procedures the book has merit, but it can scarcely be said to be up-to-date.

Studies from The Rockefeller Institute for Medical Research. Reprints. Volume 98. 597 pp. New York: The Rockefeller Institute for Medical Research. 1936.

This volume of reprints contains, among many others, a series of reports on the etiology of rabbit pox, equine encephalomyelitis, and coryza of fowl. A further report of the studies by Page on nephritis is presented, as is an interesting report on pneumothorax therapy in lobar pneumonia by Abernethy et al.

Parenteral Therapy. A Ready Reference Manual of Extra-Oral Medication for Physicians, Dentists, Pharmacists, Chemists, Biologists, Nurses, Medical Students and Veterinarians. Walton Forest Dutton and George Burt Lake. 386 pp. Baltimore and Springfield: Charles C Thomas. $7.50.

This book may be described as the "how" of medicine. Practically every technic requiring the use of the "needle" is described. Numerous illustrations clarify the text to a considerable extent. This portion comprising 160 pages should prove of value especially to practitioners whose interests are broad enough to include the various mechanical procedures employing the "needle" in diagnosis and therapy. In this effort the authors have been successful.

The remaining 200 pages are devoted to a therapeutic index and pharmacologic notes with particular reference to medicaments parenterally administered. To the reviewer it appears that much of this material is supererogatory, being a repetition of what may be found in textbooks of pharmacology, yet lacking the conservative and judicious evaluation. There is far too great a tendency for physicians to resort to "active" therapy. A great deal of this is the result of the constant bombardment by the pharmaceutical houses. It is to the detriment of this book that it makes little effort to neutralize this tendency to "ampoule" therapy. Considered by itself the first portion may be regarded the "vade mecum" of parenteral technic.

A Guide to Psychiatric Nursing. F. A. Carmichael and John Chapman. Second Edition, Thoroughly Revised. 175 pp. Philadelphia: Lea & Febiger. $2.25.

The authors would have done better to have thought out clearly the field of training to be covered and the group of students to be instructed, and then written accordingly. As it is they jump from Freud to fleas and from excretions to ethics.

"Although at birth the infant is anatomically though not sexually mature and, therefore, has no drive from the reproduction instinct, he nevertheless has undifferentiated sexual wishes . . .

"It is well to learn first-aid treatment and bandaging from some source; if no other is available the Boy Scout Handbook contains a number of things that even seasoned nurses need to know . . .

"With regard to the psychiatric treatment and nursing of patients there is a great deal to be stated, but very little that is determined."

If this book is a primer for untrained attendants much of the reading matter is beyond their scope—if it is designed for nurses already trained in the ground work of physical care much of the reading matter might well be omitted. As in many fields of instruction, definition is necessary for elucidation. This book lacks definition, and consequently stumbles in elucidation.

Endocrine Tumours and Other Essays. Frederick Parkes Weber. 207 pp. London: H. K. Lewis & Co., Ltd. 7s. 6d. net.

Dr. F. Parkes Weber has long been known in London for his wide knowledge of the bizarre and unusual in medicine. For years he has presented to the Royal Society of Medicine and other scientific bodies, patients with rare endocrine, skeletal, skin or neurological syndromes. Blood diseases have also been of special interest to him. His reports, widely scattered in medical journals, have been repeatedly published in book form and are known to clinicians and students of medical history throughout the world. All have been of interest and many have thrown new light on some of the most obscure problems of medicine. The present volume is no exception. The longest essay (on endocrine tumors), although first published in 1929, and in 1933, has been brought up to date to include the literature of 1935. Other chapters deal with hereditary diseases, paroxysmal salivation, hypersplenism, Buerger's disease, chronic erythema of the legs, and more general topics, such as classification of diseases, constipation, myths and dreams. These diffuse essays, each a brilliant exposition of a phase of medicine, are highly readable and instructive.

Doctor of the North Country. Earl Vinton McComb. 238 pp. New York: Thomas Y. Crowell Company. $2.00.

This is a well-written collection of the sort of stories from his personal experiences, that the average busy physician could tell. McComb has an unusual sense of dramatic values, so that he has made the very most of many a sordid and seamy situation.

The same painful yet humorous aspects of life with which many of us are all too familiar make a fabric permeated with the bright colors of a sensible idealism and self-sacrifice.

The most interesting chapter is that dealing most sympathetically with a physician-father, and his influence on a plastic youth leading to the study of medicine.

The reader of this novel type of physician's personal narrative, with its salty speech and life-like descriptions, lays down the book with honest regret.

Pediatric Treatment. A manual of the treatment of the diseases of infants and children designed as a reference work especially for the General Practitioner and Physicians entering the field of pediatrics. Philip S. Potter. 578 pp. New York: The Macmillan Company. $5.00.

This is a treatise on pediatrics with special emphasis upon treatment. The text consists of 540 pages with fifteen pages of additional prescriptions. It is divided into four sections as follows: (1) Therapeutic Procedures; (2) Nutrition; (3) Treatment of the Diseases and Abnormalities of the Newborn; (4) Treatment of Disease, which in turn is divided into the various body systems.

The author has recognized a definite need in attempting "to present in logical order the fundamentals of pediatric treatment for the general practitioner" — a most difficult task. He has incorporated, however, so much that is unimportant, compiled from his personal experience and from textbooks, that the book fails in its real purpose. Acute bronchitis, for instance, is treated in three stages with suggested drugs, a practice which for the most part has been found unnecessary. The same criticism is made of the chapters on artificial feeding, which contain many impractical statements, such as, "Certified milk is the only milk which can be used with comparative safety in large communities" and milk sugar "is preferable in normal conditions of infant feeding."

This book does contain many valuable therapeutic suggestions, both old and modern, and is an excellent reference for a physician with experience and a critical opinion. It lacks a chapter upon the subject which concerns the practitioner most, namely, child behavior.

Pediatric Nursing. John Zahorsky. 568 pp. St. Louis: The C. V. Mosby Company. $3.00.

Dr. Zahorsky advocates not only a thorough knowledge of the procedures and technics necessary for the intelligent care of an ill child, but a detailed knowledge of the growth, development, and management of the normal well child. The first chapters of his book deal briefly, but concisely, with this aspect of pediatrics. Following this is a chapter stressing the prevention of diseases in baby- and childhood which is most commendable, and a phase which is all too often left unmentioned in textbooks for nurses. Dr. Zahorsky also devotes a chapter to the importance of training a pediatric nurse to observe not only symptoms and abnormalities of sickness, but the signs and features of the well and normal child.

Next, he takes up the diseases of infancy and childhood, grouping them under several headings, such as Diseases of Digestive System, Respiratory Organs, Bones and Joints, Deficiency Diseases, and so forth. This part of the book seems to be a little too brief. Each disease is disposed of in a paragraph or two, and for this reason its value as a textbook would seem limited. The inclusion of the common contagious diseases of childhood is an excellent feature.

The chapters given over to the equipment and materials needed in a pediatric unit of a hospital seem somewhat unnecessary in a book of this type, and the space used for this could be more profitably used in giving a more detailed picture of the common and serious illnesses a nurse would encounter in her care of babies and children.

The final chapters of the book, devoted to procedures used not only in the hospital but in the home as well, are of very great value and well presented. The illustrations are numerous, well chosen and are assets to the book as a whole.

The book seems especially adapted for a reference book for the graduate nurse, but anyone—student nurse, graduate nurse, or even a lay person—who is caring for a child or children will find a great deal of assistance and value in this book.

Principles and Practice of Recreational Therapy for the Mentally Ill. John Eisele Davis. In collaboration with William Rush Dunton, Jr. 206 pp. New York: A. S. Barnes & Company. $3.00.

Although occupational therapy has long played a valuable part in treating the mentally ill, organized recreation with the same aim in mind has never been adequately recognized. The author of this book, who has had wide experience in a veterans' hospital for mental disease, has for the first time brought together the details of recreational therapy. The opening chapter is an excellent résumé of the types of disease found in a mental hospital. This is followed by details of recreational activities, with particular attention given to those types of play which are best suited for patients with dementia praecox, encephalitis, paranoia, etc. The author does not attempt to evaluate the effect of recreational therapy; he simply states the essence of the various games and tests and, in the final chapter, outlines the aims and objectives. This book, extremely well written, will serve as a foundation for work in many hospitals. Ultimately we shall be able to draw some conclusions in regard to whether or not such detailed recreational work is worth while.

Bewildered Patient. Marian S. Newcomer. 323 pp. Boston and New York: Hale Cushman & Flint. $1.75.

The bewildered patient tends to dramatize too strongly the very information medical men would like their patients to have. Much of the material has already been published in lay magazines where it is more certain to be found by the average layman. Like many, in the flood of books by doctors pouring out today, it would be far better as a simple pamphlet, without the "school ma'am" attitude that most women doctors exhibit.